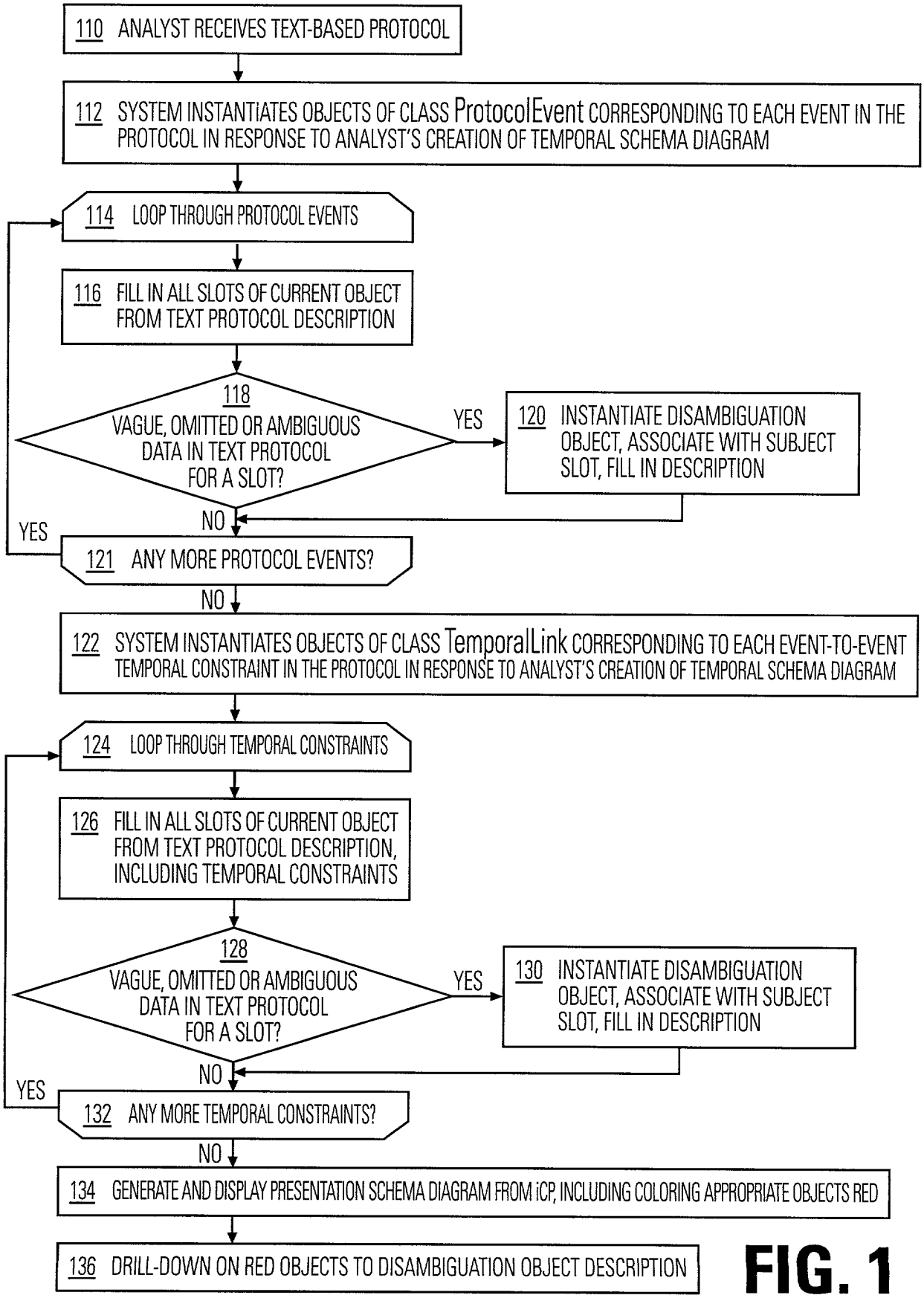

FIG. 1

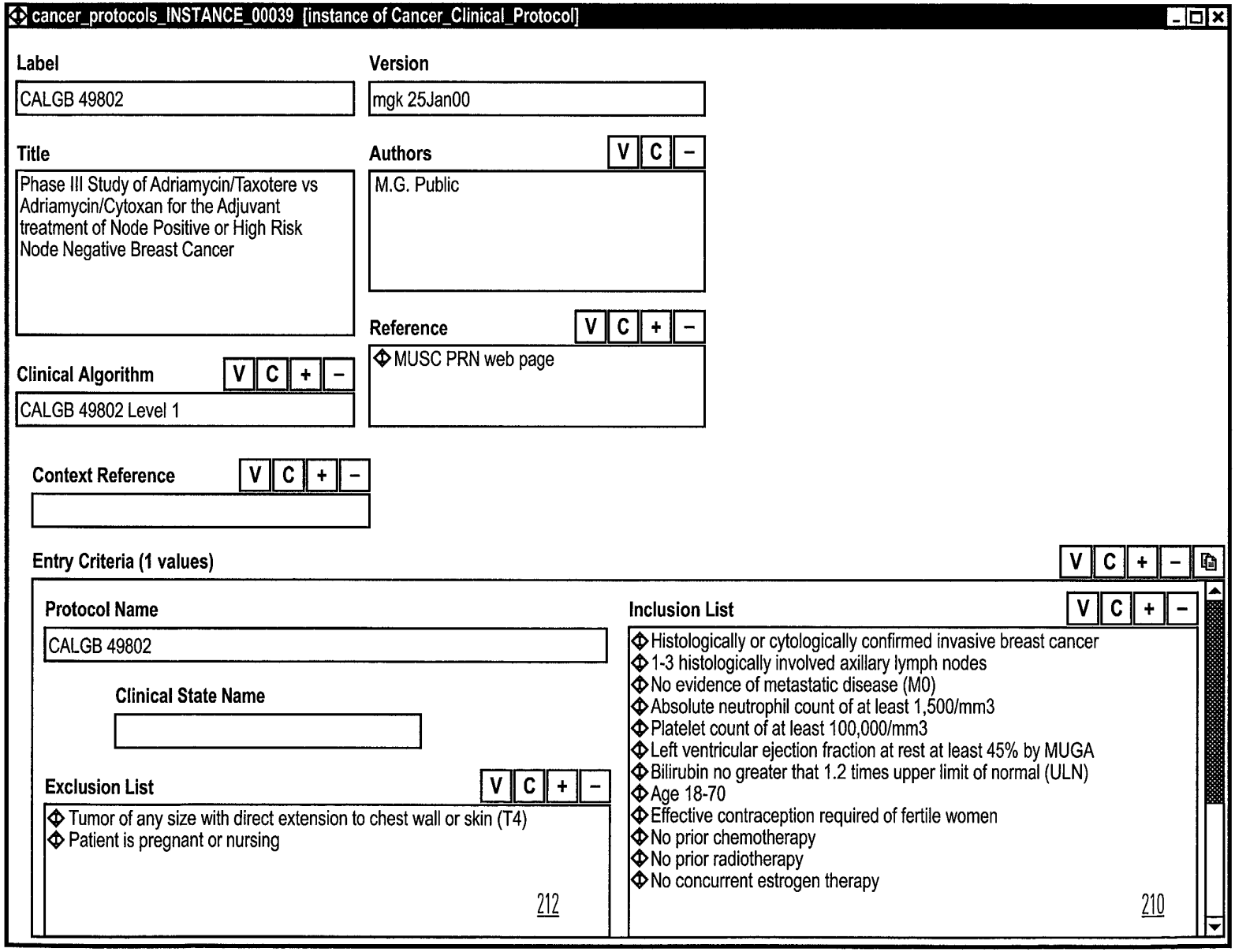
cancer_protocols_INSTANCE_00039 [instance of Cancer_Clinical_Protocol]
Label
CALGB 49802
Version
mgk 25Jan00
Title
Phase III Study of Adriamycin/Taxotere vs Adriamycin/Cytoxan for the Adjuvant treatment of Node Positive or High Risk Node Negative Breast Cancer
Authors
V C –
M.G. Public
Reference
V C + –
MUSC PRN web page
Clinical Algorithm
V C + –
CALGB 49802 Level 1
Context Reference
V C + –
Entry Criteria (1 values)
V C + –
Protocol Name
CALGB 49802
Clinical State Name
Exclusion List
V C + –
Tumor of any size with direct extension to chest wall or skin (T4)
Patient is pregnant or nursing
212
Inclusion List
V C + –
Histologically or cytologically confirmed invasive breast cancer
1-3 histologically involved axillary lymph nodes
No evidence of metastatic disease (M0)
Absolute neutrophil count of at least 1,500/mm3
Platelet count of at least 100,000/mm3
Left ventricular ejection fraction at rest at least 45% by MUGA
Bilirubin no greater that 1.2 times upper limit of normal (ULN)
Age 18-70
Effective contraception required of fertile women
No prior chemotherapy
No prior radiotherapy
No concurrent estrogen therapy
210

FIG. 2

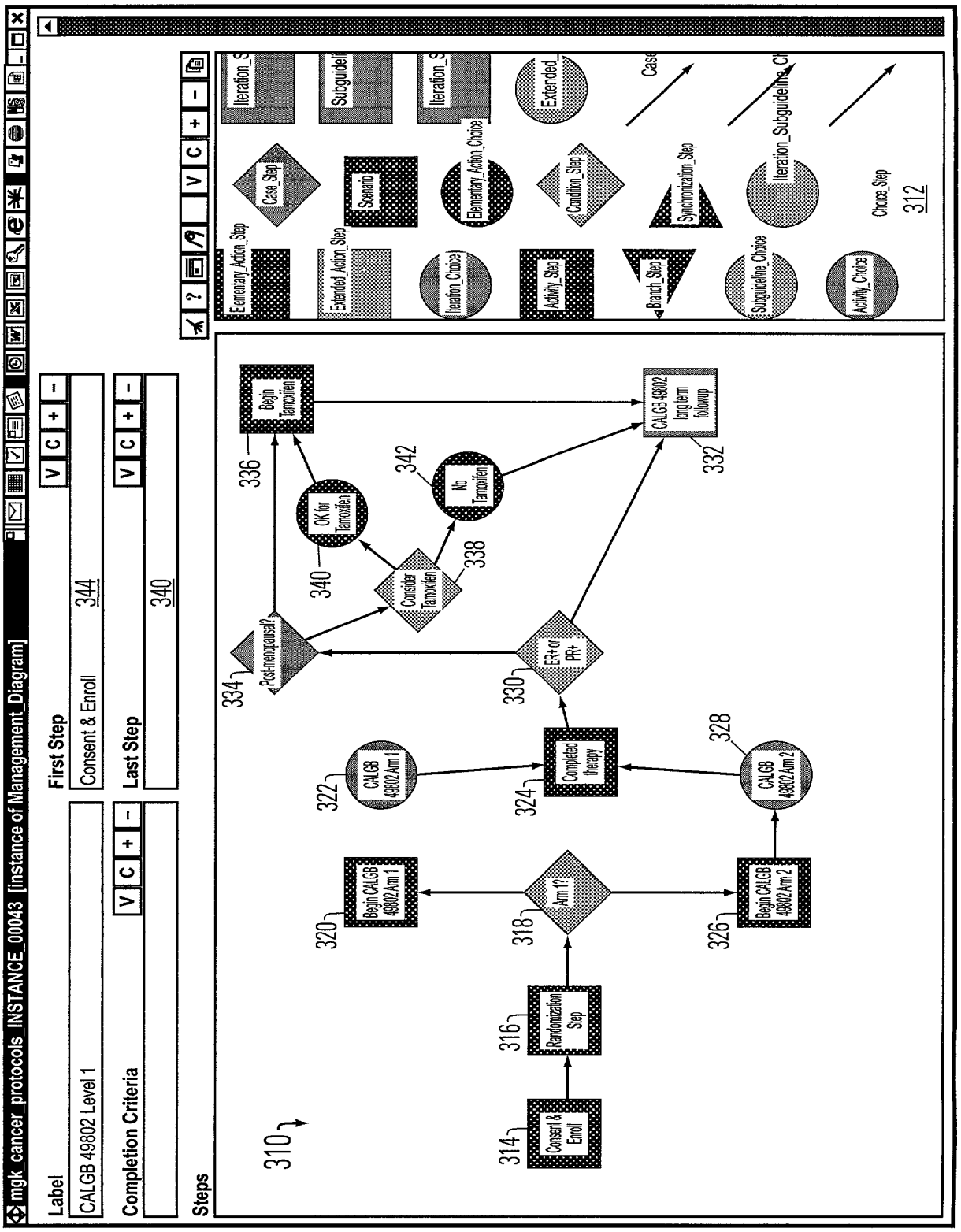
mgk_cancer_protocols_INSTANCE_00043 [instance of Management_Diagram]
Label
CALGB 49802 Level 1
Completion Criteria
Steps
First Step
Consent & Enroll
344
Last Step
340
310
Consent & Enroll
314
Randomization Step
316
Arm 1?
318
Begin CALGB 49802 Arm 1
320
CALGB 49802 Arm 1
322
Begin CALGB 49802 Arm 2
326
CALGB 49802 Arm 2
328
Completed therapy
324
ER+ or PR+
330
Post-menopausal?
334
Consider Tamoxifen
338
OK for Tamoxifen
340
No Tamoxifen
342
Begin Tamoxifen
336
CALGB 49802 long term followup
332
Elementary_Action_Step
Extended_Action_Step
Iteration_Choice
Case_Step
Scenario
Elementary_Action_Choice
Activity_Step
Condition_Step
Branch_Step
Synchronization_Step
Subguideline_Choice
Iteration_Subguideline_Ch
Activity_Choice
Choice_Step
312

FIG. 3

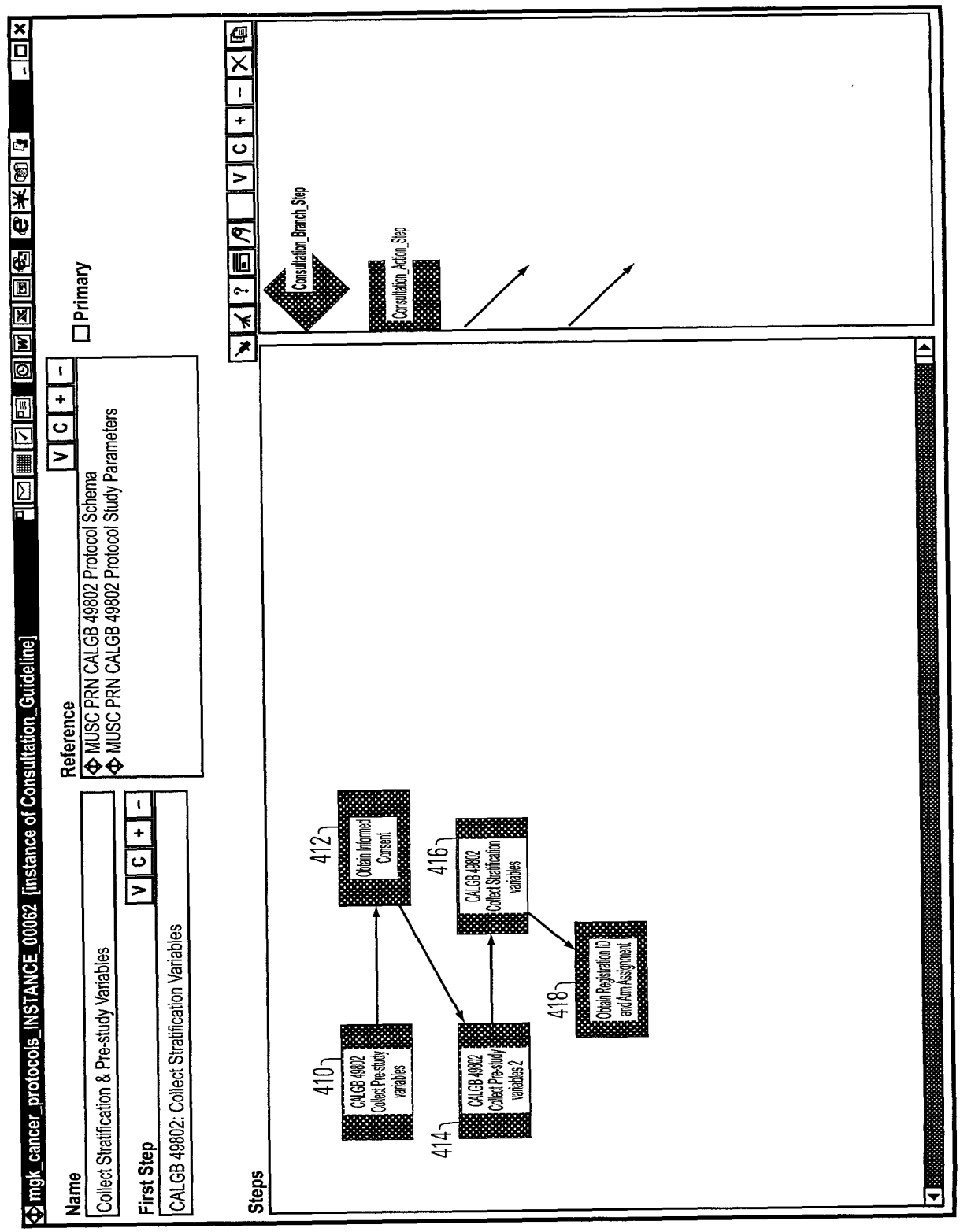
mgk_cancer_protocols_INSTANCE_00062 [instance of Consultation_Guideline]
Name
Collect Stratification & Pre-study Variables
First Step
CALGB 49802: Collect Stratification Variables
Reference
MUSC PRN CALGB 49802 Protocol Schema
MUSC PRN CALGB 49802 Protocol Study Parameters
Primary
Steps
Consultation_Branch_Step
Consultation_Action_Step
412
Obtain Informed Consent
410
CALGB 49802 Collect Pre-study variables
414
CALGB 49802 Collect Pre-study variables 2
416
CALGB 49802 Collect Stratification variables
418
Obtain Registration ID and Arm Assignment

FIG. 4

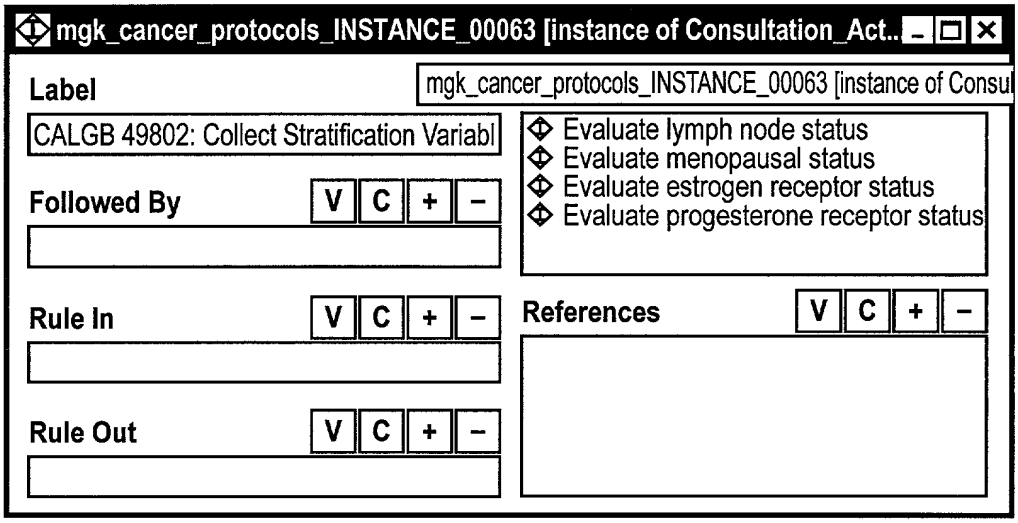
mgk_cancer_protocols_INSTANCE_00063 [instance of Consultation_Act..
Label
mgk_cancer_protocols_INSTANCE_00063 [instance of Consul
CALGB 49802: Collect Stratification Variabl
Evaluate lymph node status
Evaluate menopausal status
Evaluate estrogen receptor status
Evaluate progesterone receptor status
Followed By
V C + –
Rule In
V C + –
References
V C + –
Rule Out
V C + –

FIG. 5

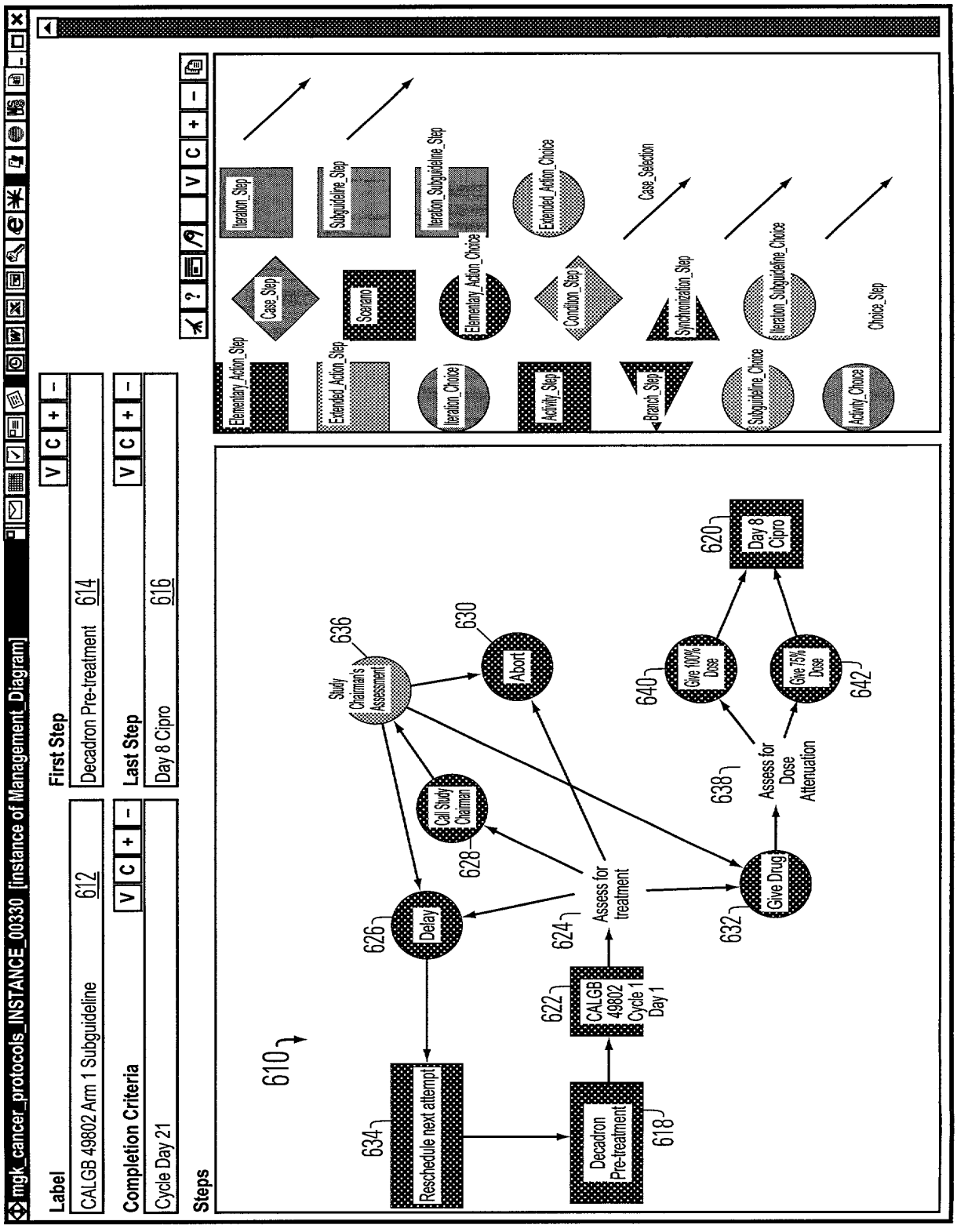
mgk_cancer_protocols_INSTANCE_00330 [instance of Management_Diagram]
Label
CALGB 49802 Arm 1 Subguideline
612
First Step
Decadron Pre-treatment
614
Completion Criteria
Cycle Day 21
Last Step
Day 8 Cipro
616
Steps
610
Elementary_Action_Step
Extended_Action_Step
Case_Step
Scenario
Iteration_Choice
Elementary_Action_Choice
Activity_Step
Condition_Step
Branch_Step
Synchronization_Step
Iteration_Step
Subguideline_Step
Iteration_Subguideline_Step
Extended_Action_Choice
Case_Selection
Subguideline_Choice
Iteration_Subguideline_Choice
Activity_Choice
Choice_Step
634
Reschedule next attempt
618
Decadron Pre-treatment
622
CALGB 49802 Cycle 1 Day 1
624
Assess for treatment
626
Delay
628
Call Study Chairman
636
Study Chairman's Assessment
630
Abort
632
Give Drug
638
Assess for Dose Attenuation
640
Give 100% Dose
642
Give 75% Dose
620
Day 8 Cipro

FIG. 6

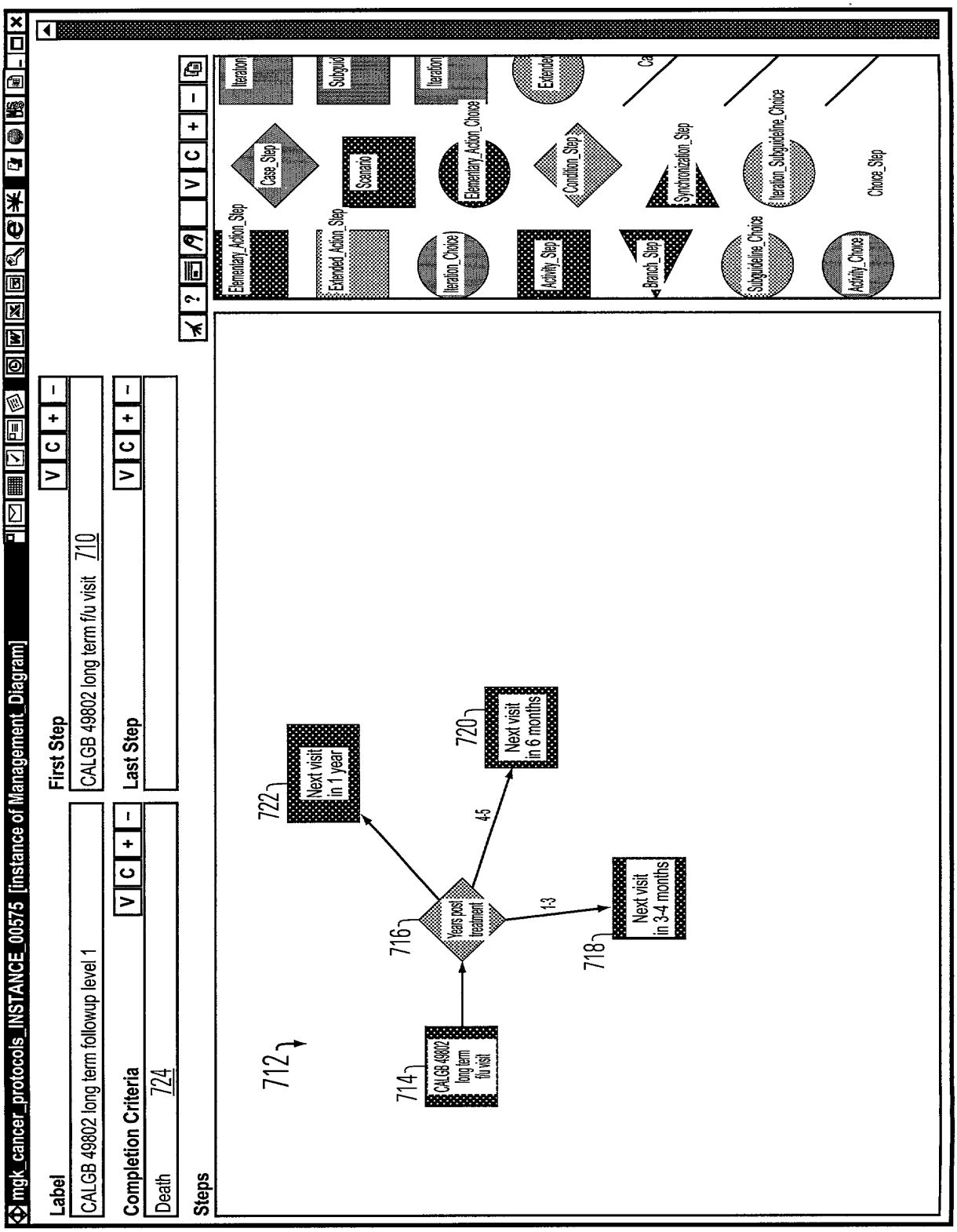
mgk_cancer_protocols_INSTANCE_00575 [instance of Management_Diagram]
Label
CALGB 49802 long term followup level 1
Completion Criteria
Death
724
Steps
First Step
CALGB 49802 long term f/u visit
710
Last Step
712
714
CALGB 49802 long term f/u visit
716
Years post treatment
718
Next visit in 3-4 months
720
Next visit in 6 months
722
Next visit in 1 year
1-3
4-5
Elementary_Action_Step
Extended_Action_Step
Case_Step
Scenario
Iteration_Choice
Elementary_Action_Choice
Activity_Step
Condition_Step
Branch_Step
Synchronization_Step
Subguideline_Choice
Iteration_Subguideline_Choice
Activity_Choice
Choice_Step

FIG. 7

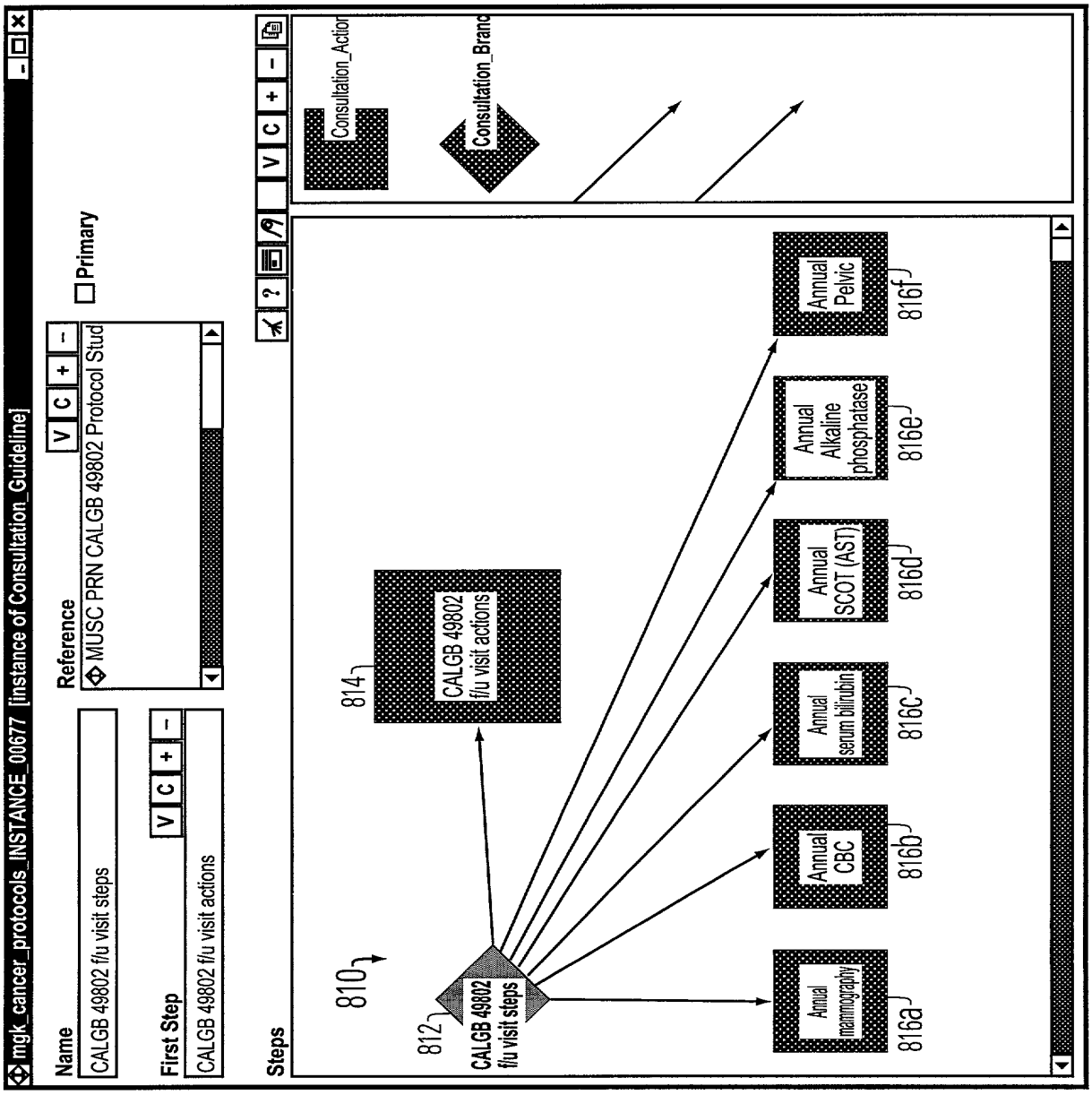
mgk_cancer_protocols_INSTANCE_00677 [instance of Consultation_Guideline]
Name
CALGB 49802 f/u visit steps
Reference
MUSC PRN CALGB 49802 Protocol Stud
Primary
First Step
CALGB 49802 f/u visit actions
Steps
Consultation_Actior
Consultation_Brand
810
812
CALGB 49802 f/u visit steps
814
CALGB 49802 f/u visit actions
Annual mammography
816a
Annual CBC
816b
Annual serum bilirubin
816c
Annual SCOT (AST)
816d
Annual Alkaline phosphatase
816e
Annual Pelvic
816f

FIG. 8

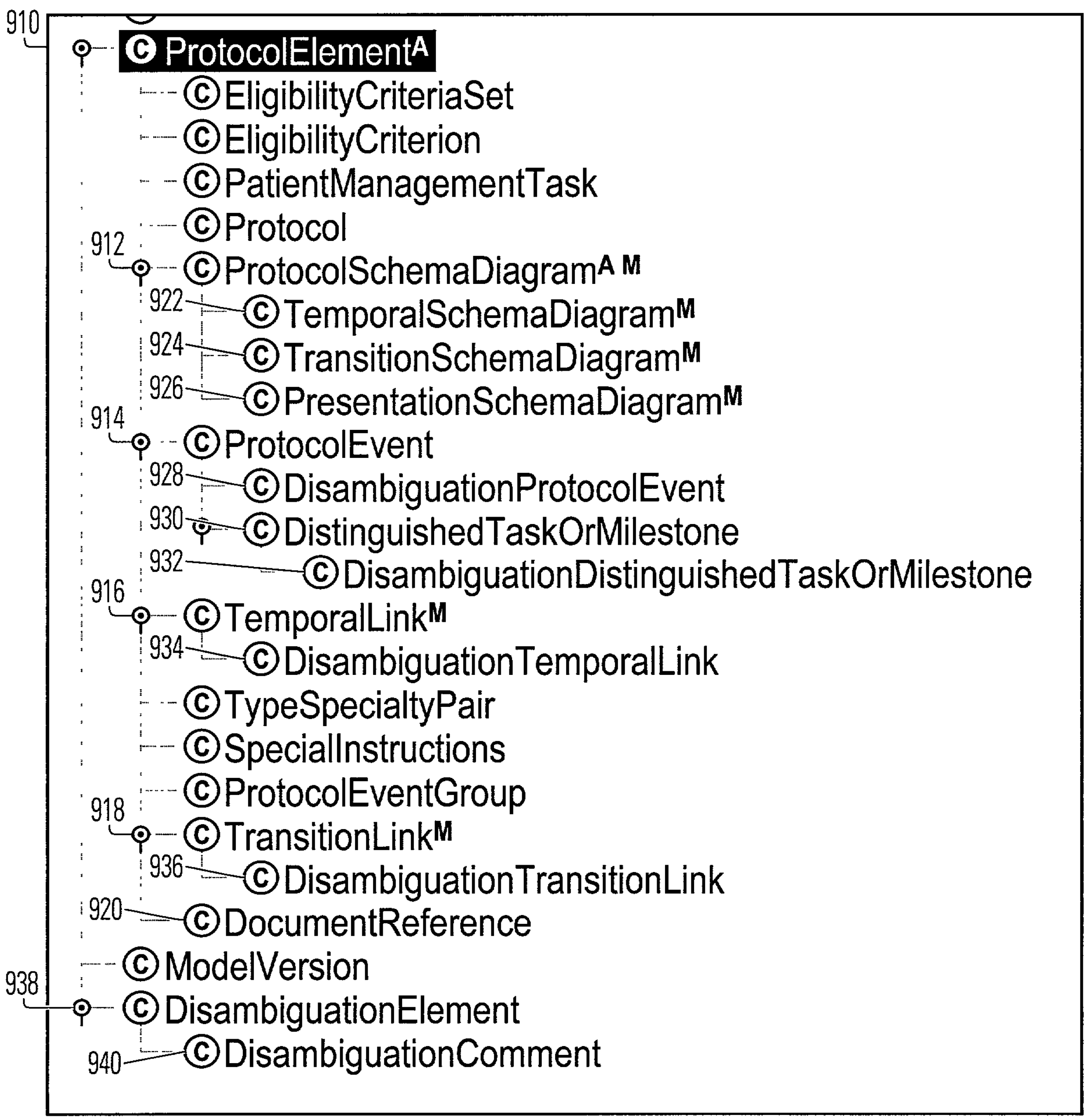

FIG. 9

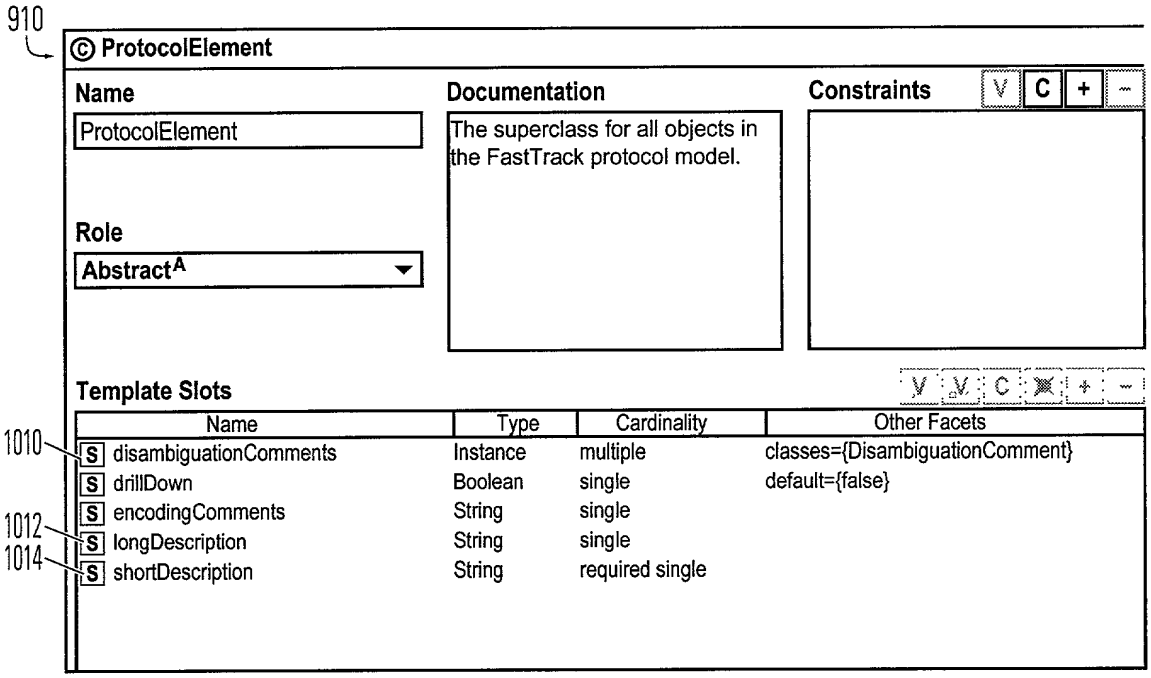
910
© ProtocolElement
Name
ProtocolElement
Documentation
The superclass for all objects in the FastTrack protocol model.
Constraints
V C + -
Role
Abstract^A
Template Slots
Name
Type
Cardinality
Other Facets
1010
S disambiguationComments
Instance
multiple
classes={DisambiguationComment}
S drillDown
Boolean
single
default={false}
1012
S encodingComments
String
single
S longDescription
String
single
1014
S shortDescription
String
required single

FIG. 10

Inventors: Michael G. Kahn et al.
Title: Protocol Disambiguation Using a Model-Based Methodology (as amended)
Application No. 09/974,781

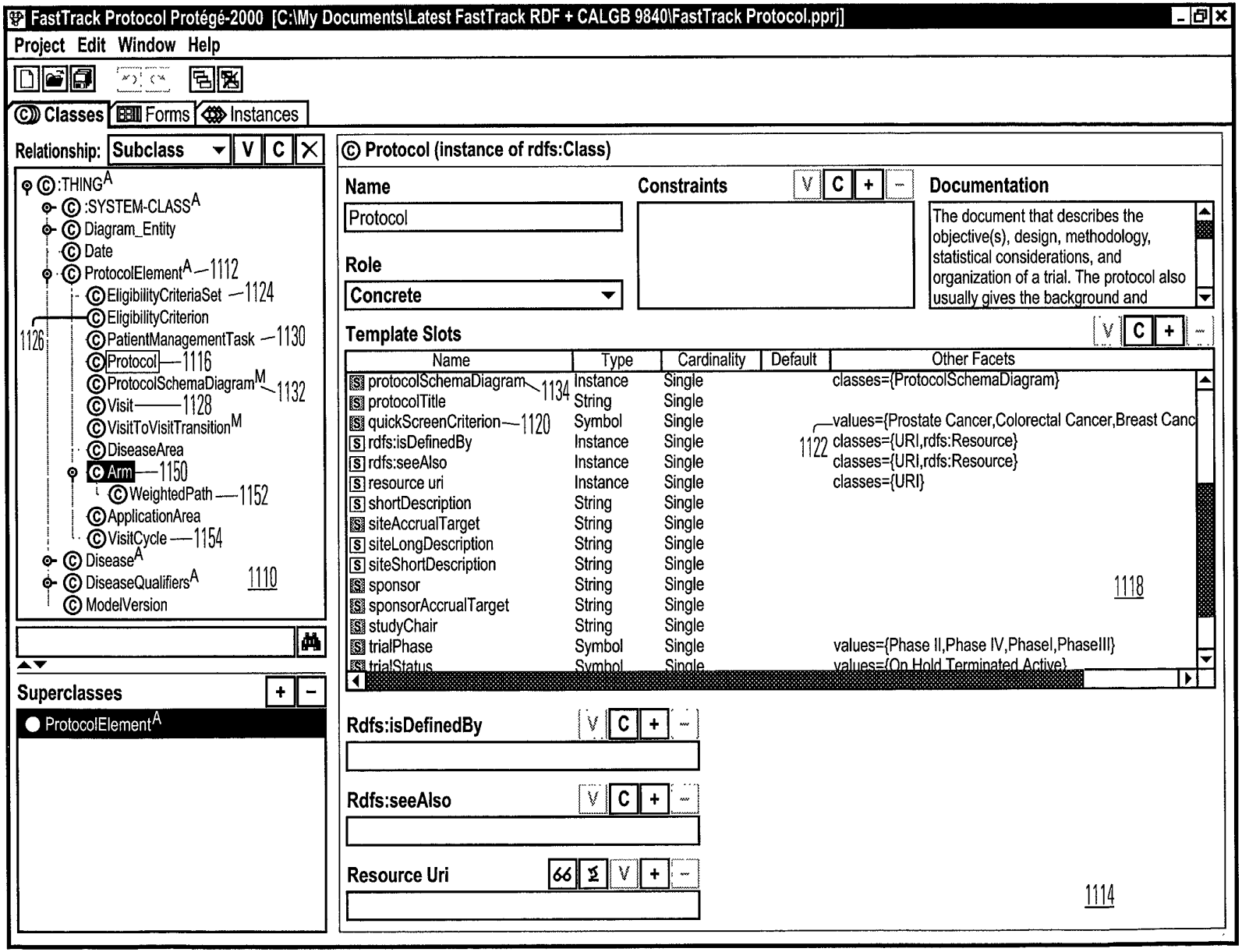

FIG. 11

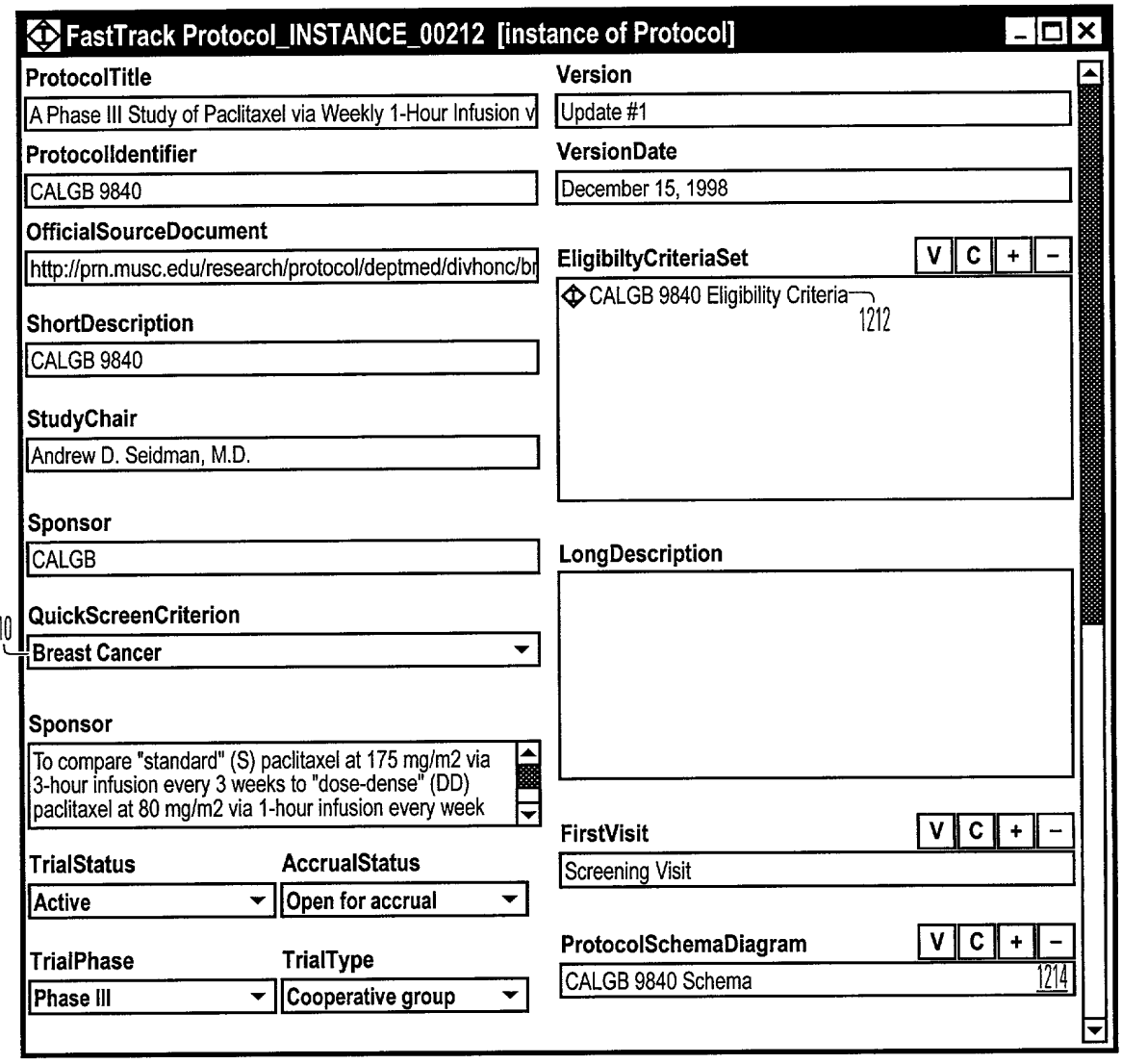
FastTrack Protocol_INSTANCE_00212 [instance of Protocol]
ProtocolTitle
A Phase III Study of Paclitaxel via Weekly 1-Hour Infusion v
ProtocolIdentifier
CALGB 9840
OfficialSourceDocument
http://prn.musc.edu/research/protocol/deptmed/divhonc/br
ShortDescription
CALGB 9840
StudyChair
Andrew D. Seidman, M.D.
Sponsor
CALGB
1210
QuickScreenCriterion
Breast Cancer
Sponsor
To compare "standard" (S) paclitaxel at 175 mg/m2 via 3-hour infusion every 3 weeks to "dose-dense" (DD) paclitaxel at 80 mg/m2 via 1-hour infusion every week
TrialStatus
Active
AccrualStatus
Open for accrual
TrialPhase
Phase III
TrialType
Cooperative group
Version
Update #1
VersionDate
December 15, 1998
EligibiltyCriteriaSet
V C + -
CALGB 9840 Eligibility Criteria
1212
LongDescription
FirstVisit
V C + -
Screening Visit
ProtocolSchemaDiagram
V C + -
CALGB 9840 Schema
1214

FIG. 12

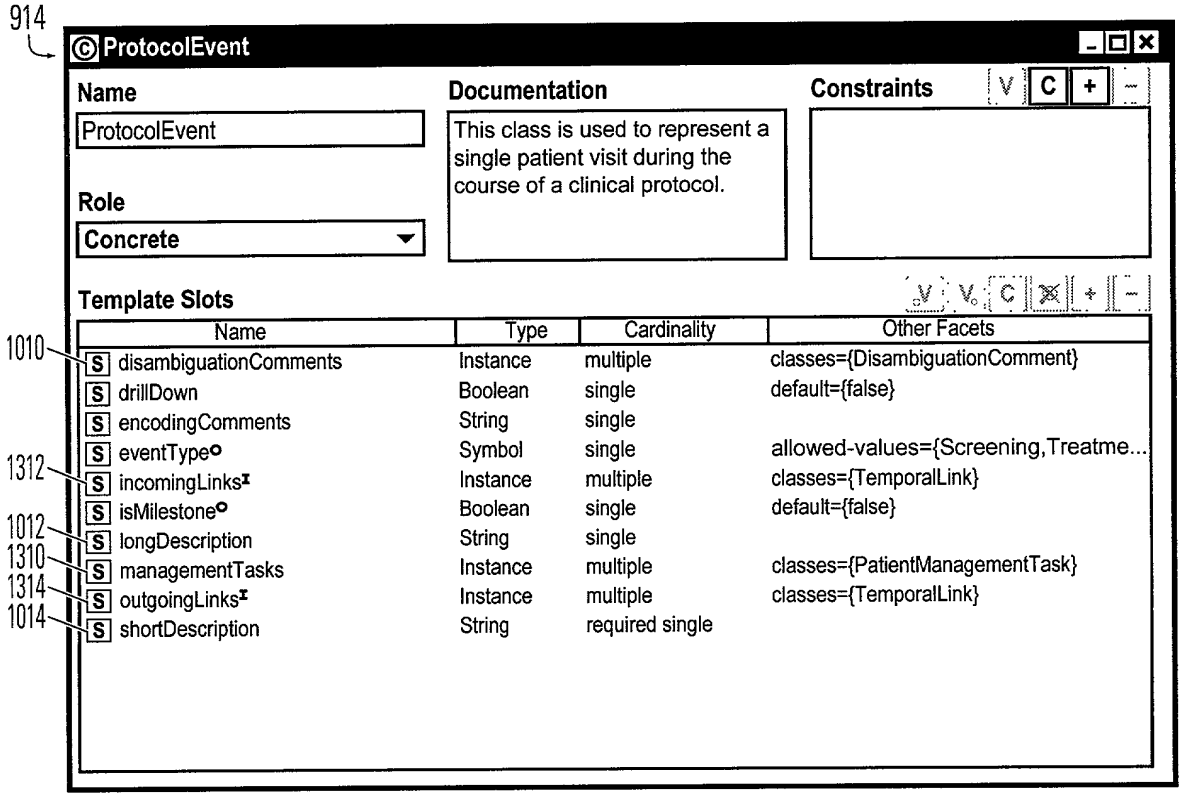
914
ProtocolEvent
Name
ProtocolEvent
Documentation
This class is used to represent a single patient visit during the course of a clinical protocol.
Constraints
Role
Concrete
Template Slots
Name
Type
Cardinality
Other Facets
1010
disambiguationComments
Instance
multiple
classes={DisambiguationComment}
drillDown
Boolean
single
default={false}
encodingComments
String
single
eventType
Symbol
single
allowed-values={Screening,Treatme...
1312
incomingLinks
Instance
multiple
classes={TemporalLink}
isMilestone
Boolean
single
default={false}
1012
longDescription
String
single
1310
managementTasks
Instance
multiple
classes={PatientManagementTask}
1314
outgoingLinks
Instance
multiple
classes={TemporalLink}
1014
shortDescription
String
required single

FIG. 13

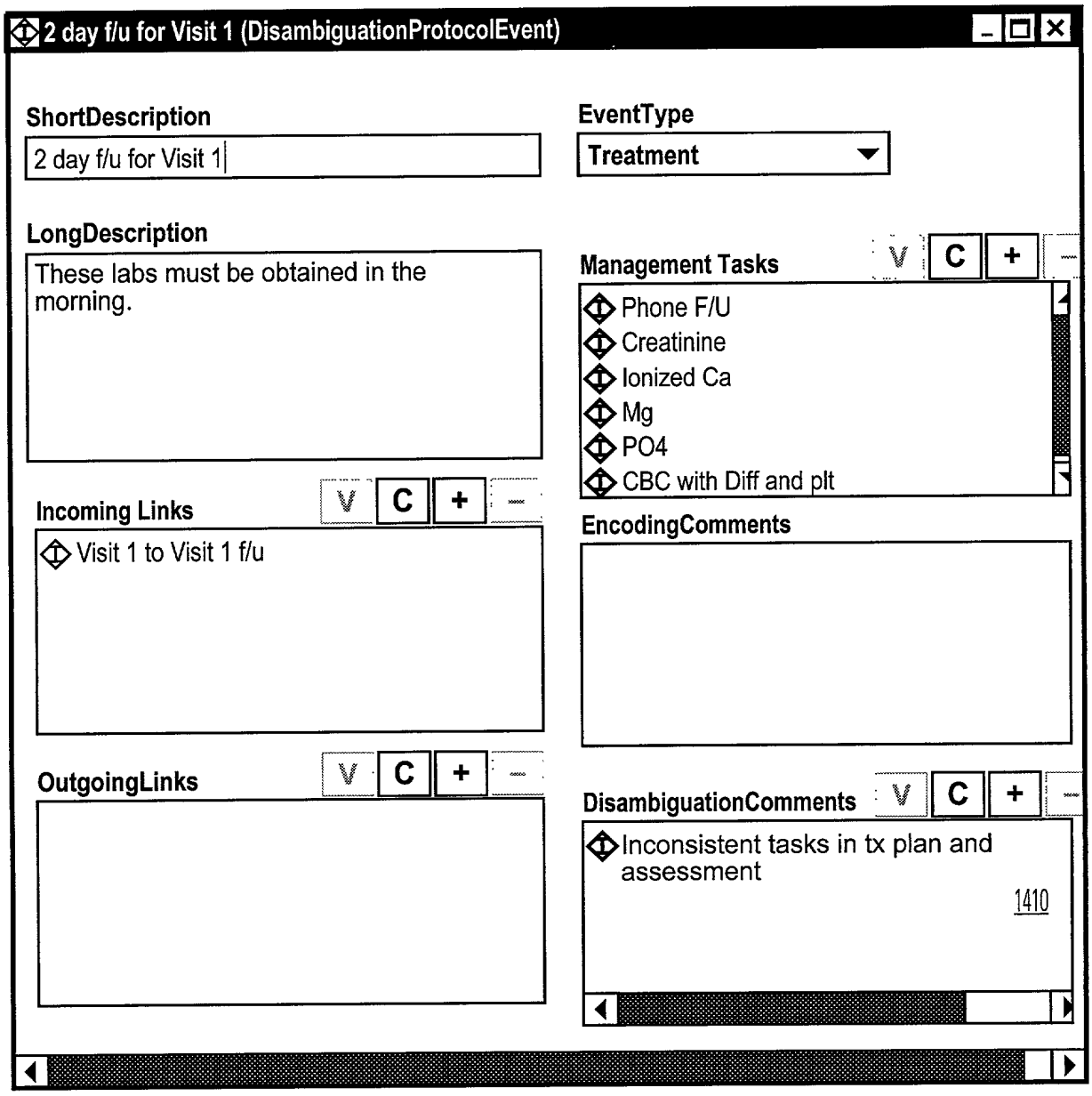
2 day f/u for Visit 1 (DisambiguationProtocolEvent)
ShortDescription
2 day f/u for Visit 1
EventType
Treatment
LongDescription
These labs must be obtained in the morning.
Management Tasks
V
C
+
Phone F/U
Creatinine
Ionized Ca
Mg
PO4
CBC with Diff and plt
Incoming Links
Visit 1 to Visit 1 f/u
EncodingComments
OutgoingLinks
DisambiguationComments
Inconsistent tasks in tx plan and assessment
1410

FIG. 14

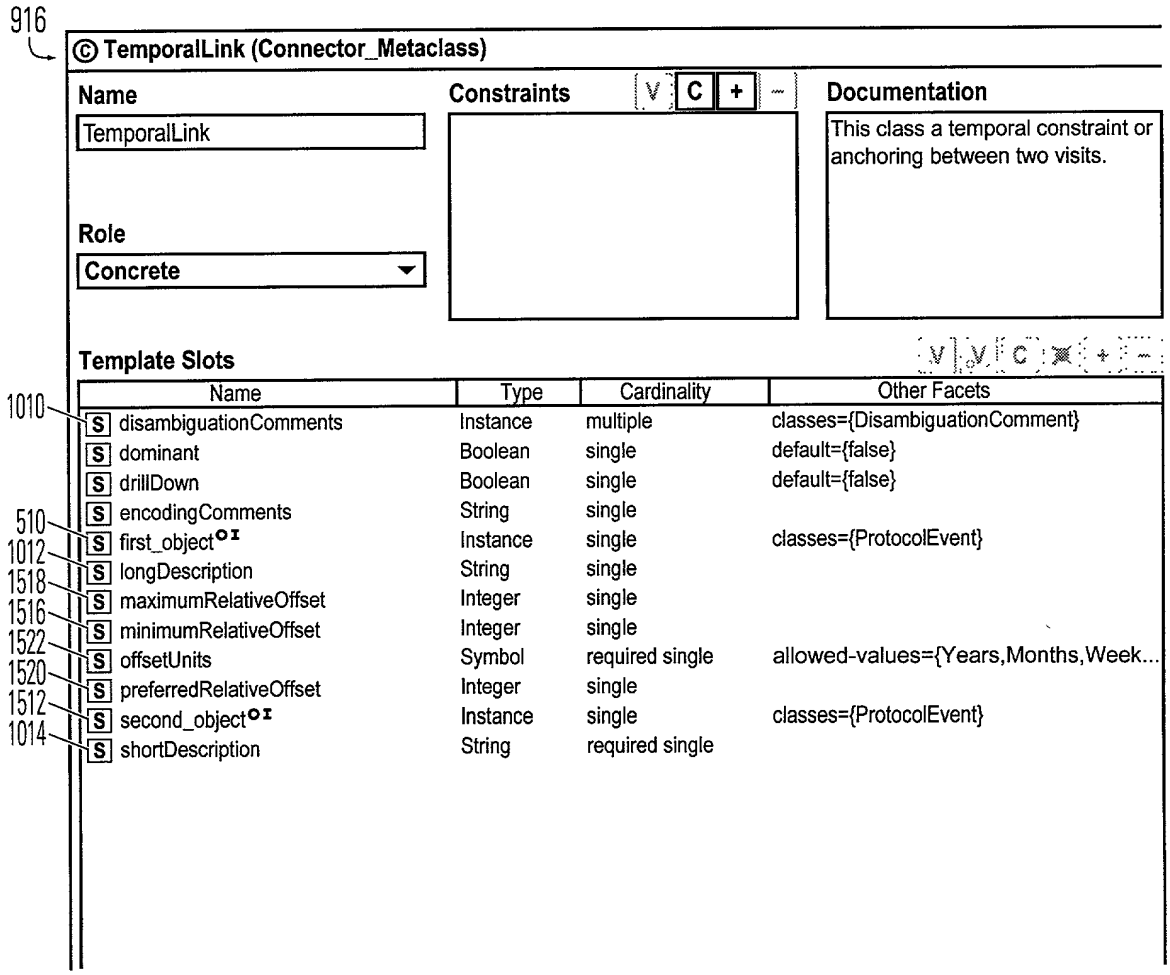
916
© TemporalLink (Connector_Metaclass)
Name
TemporalLink
Constraints
V C + -
Documentation
This class a temporal constraint or anchoring between two visits.
Role
Concrete
Template Slots
Name
Type
Cardinality
Other Facets
1010
S disambiguationComments
Instance
multiple
classes={DisambiguationComment}
S dominant
Boolean
single
default={false}
S drillDown
Boolean
single
default={false}
S encodingComments
String
single
510
S first_object OI
Instance
single
classes={ProtocolEvent}
1012
S longDescription
String
single
1518
S maximumRelativeOffset
Integer
single
1516
S minimumRelativeOffset
Integer
single
1522
S offsetUnits
Symbol
required single
allowed-values={Years,Months,Week...
1520
S preferredRelativeOffset
Integer
single
1512
S second_object OI
Instance
single
classes={ProtocolEvent}
1014
S shortDescription
String
required single

FIG. 15

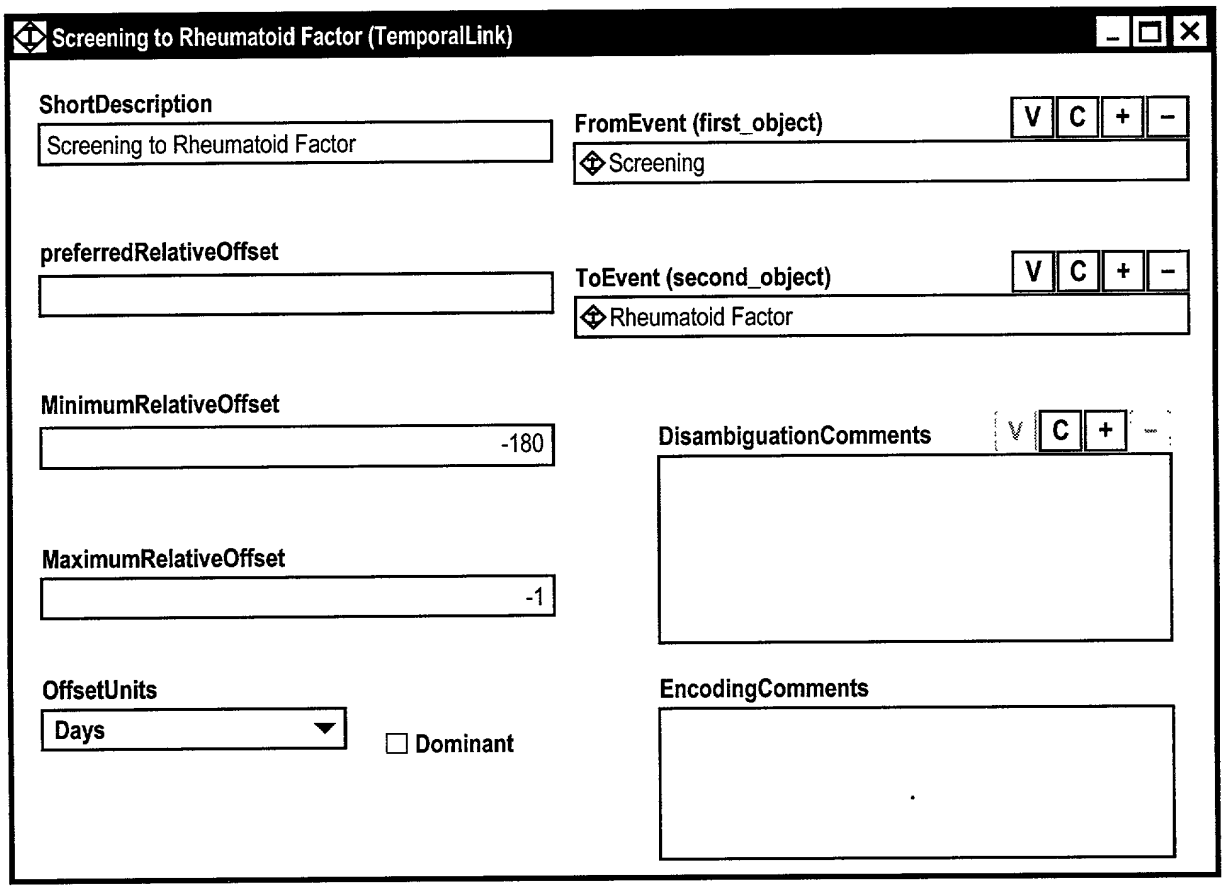
Screening to Rheumatoid Factor (TemporalLink)
ShortDescription
Screening to Rheumatoid Factor
FromEvent (first_object)
V C + -
Screening
preferredRelativeOffset
ToEvent (second_object)
V C + -
Rheumatoid Factor
MinimumRelativeOffset
-180
DisambiguationComments
V C + -
MaximumRelativeOffset
-1
OffsetUnits
Days
Dominant
EncodingComments

FIG. 16

Inventors: Michael G. Kahn et al.
Title: Protocol Disambiguation Using a Model-Based Methodology (as amended)
Application No. 09/974,781

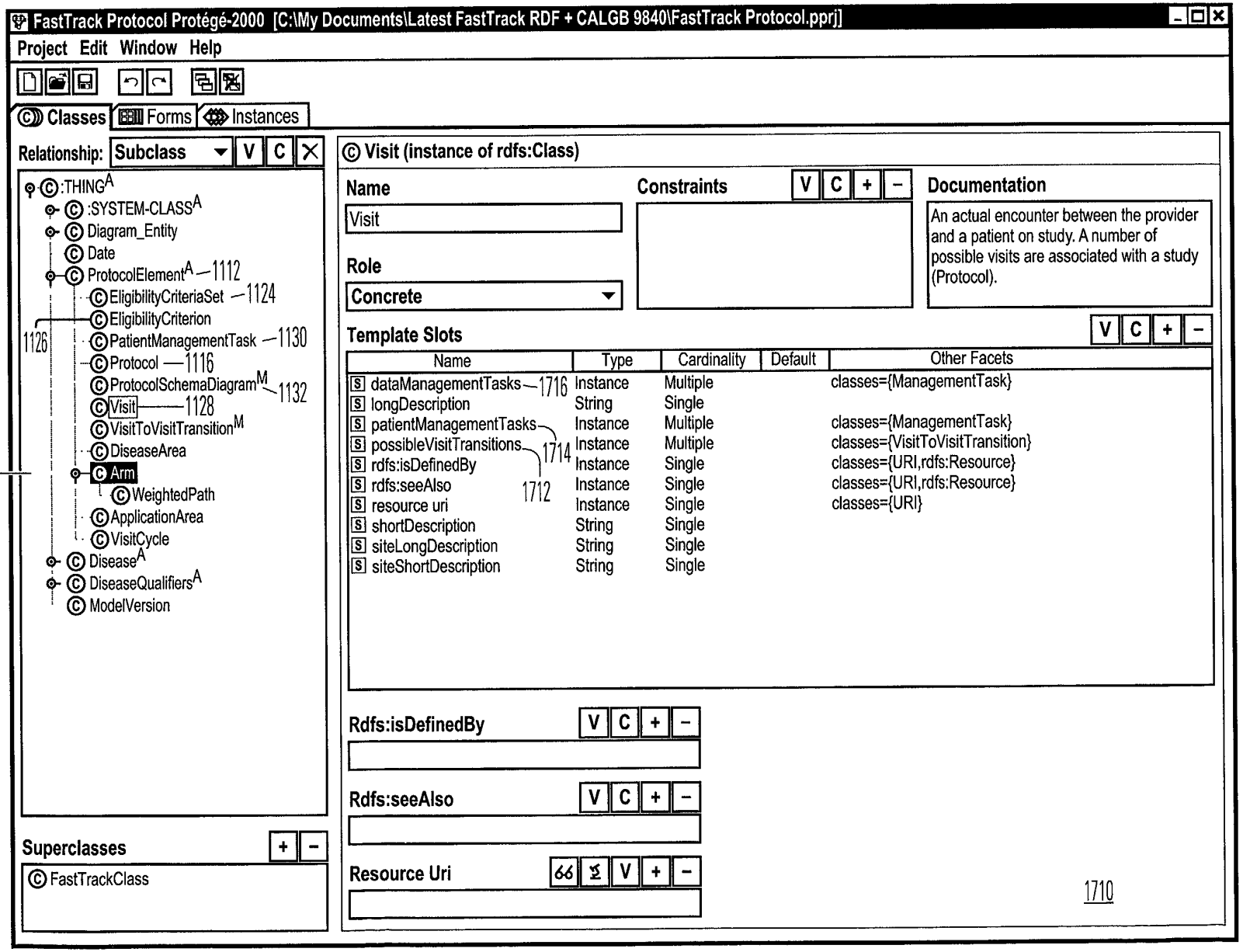

FIG. 17

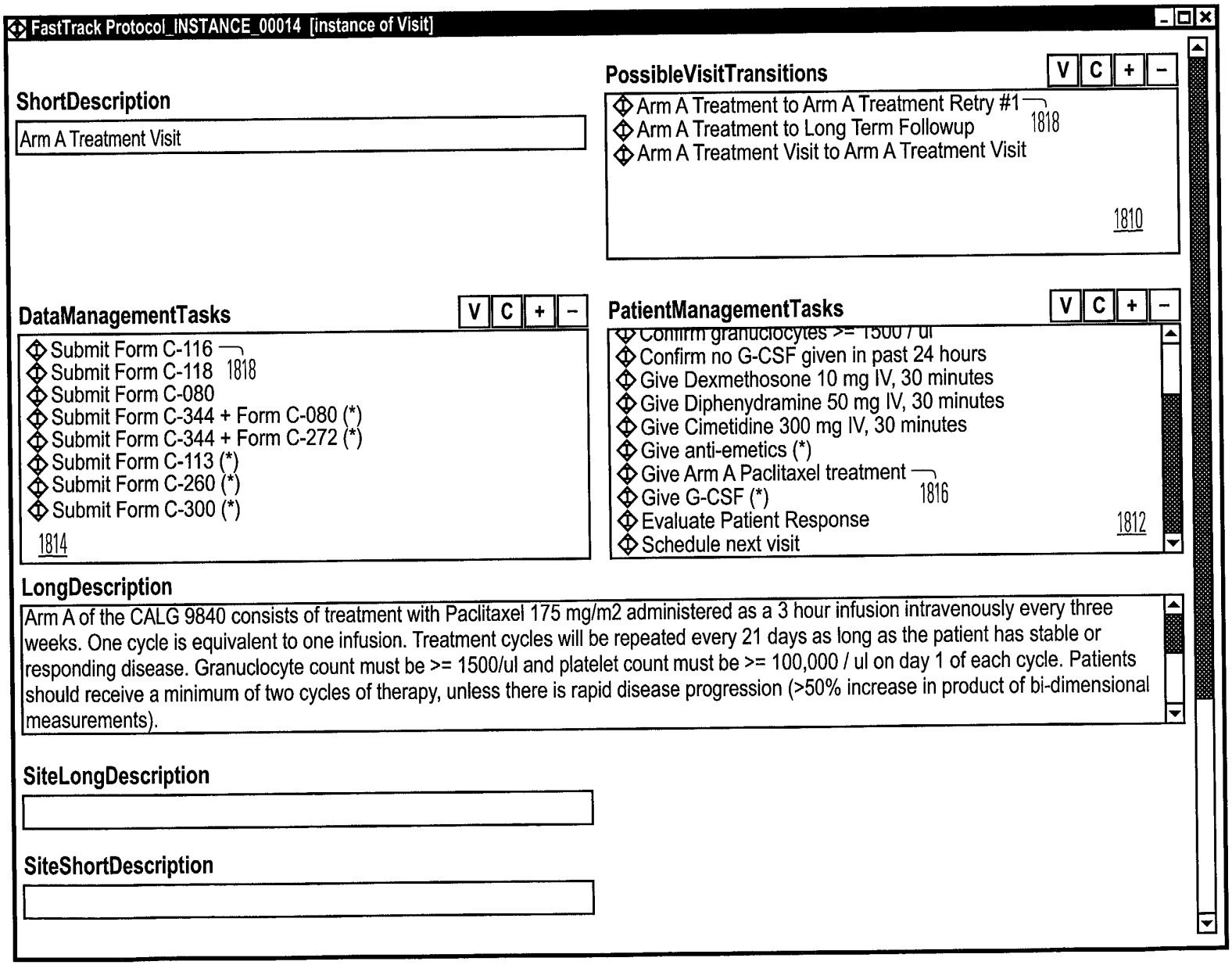

FIG. 18

Inventors: Michael G. Kahn et al.
Title: Protocol Disambiguation Using a Model-Based Methodology (as amended)
Application No. 09/974,781

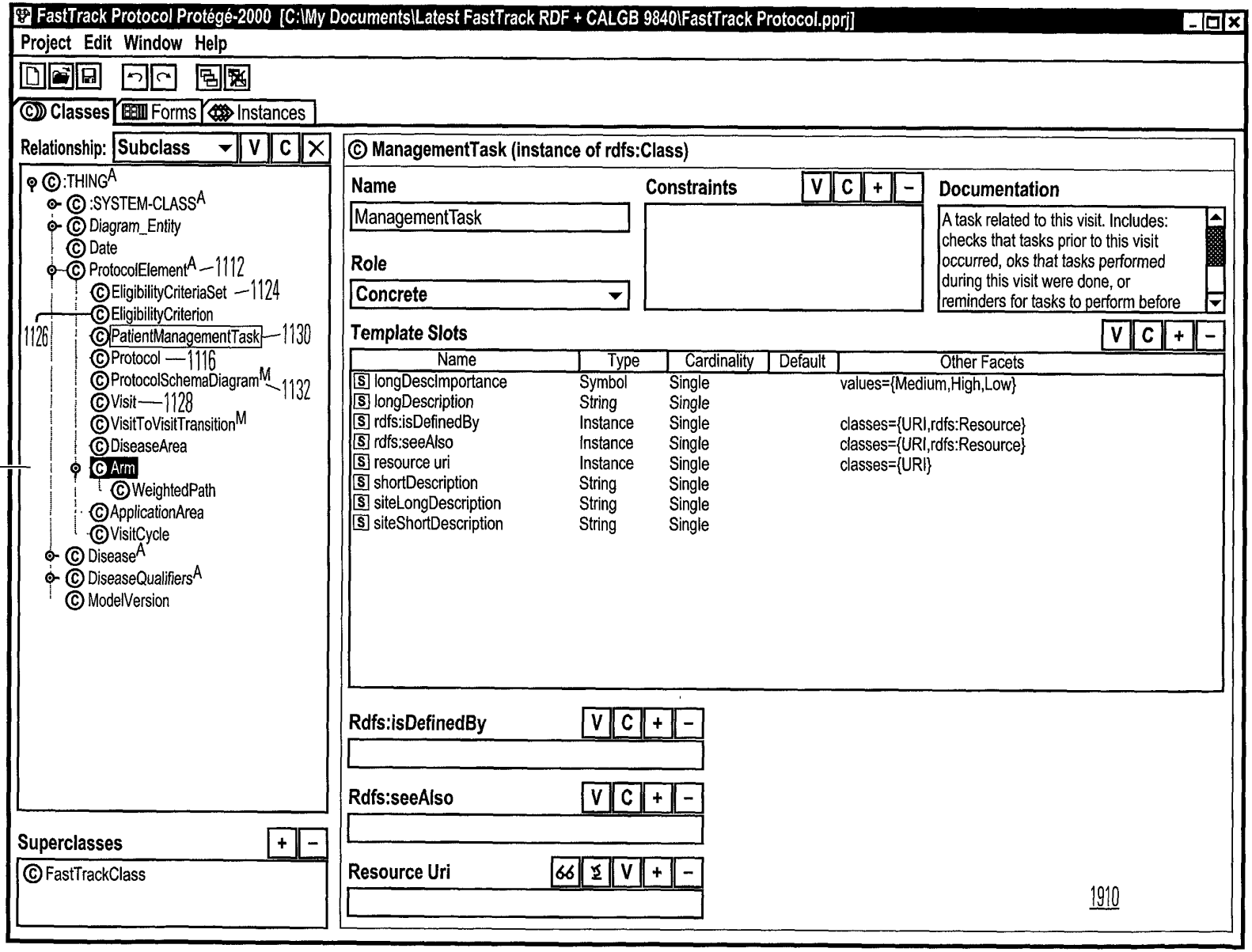

FIG. 19

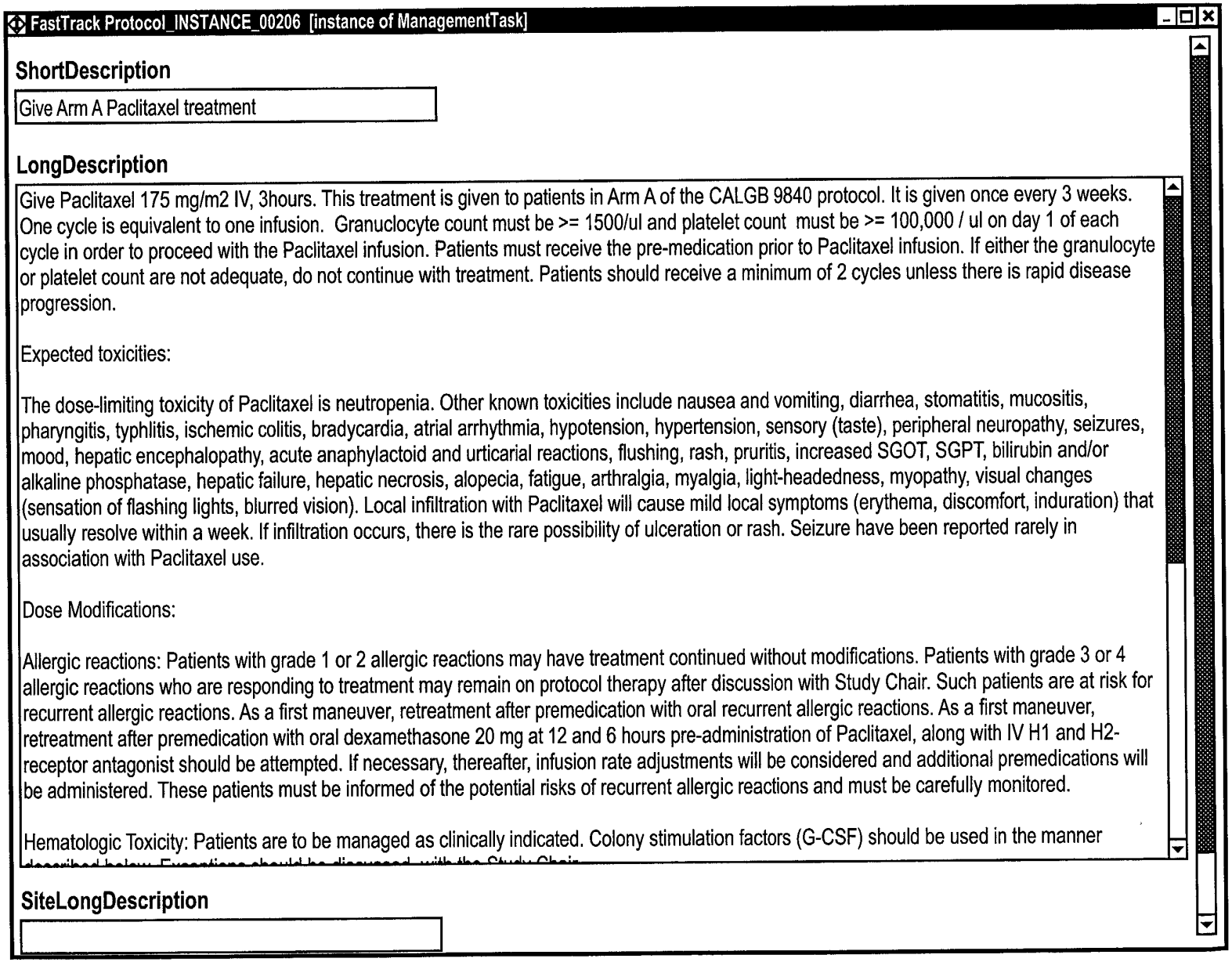

FIG. 20

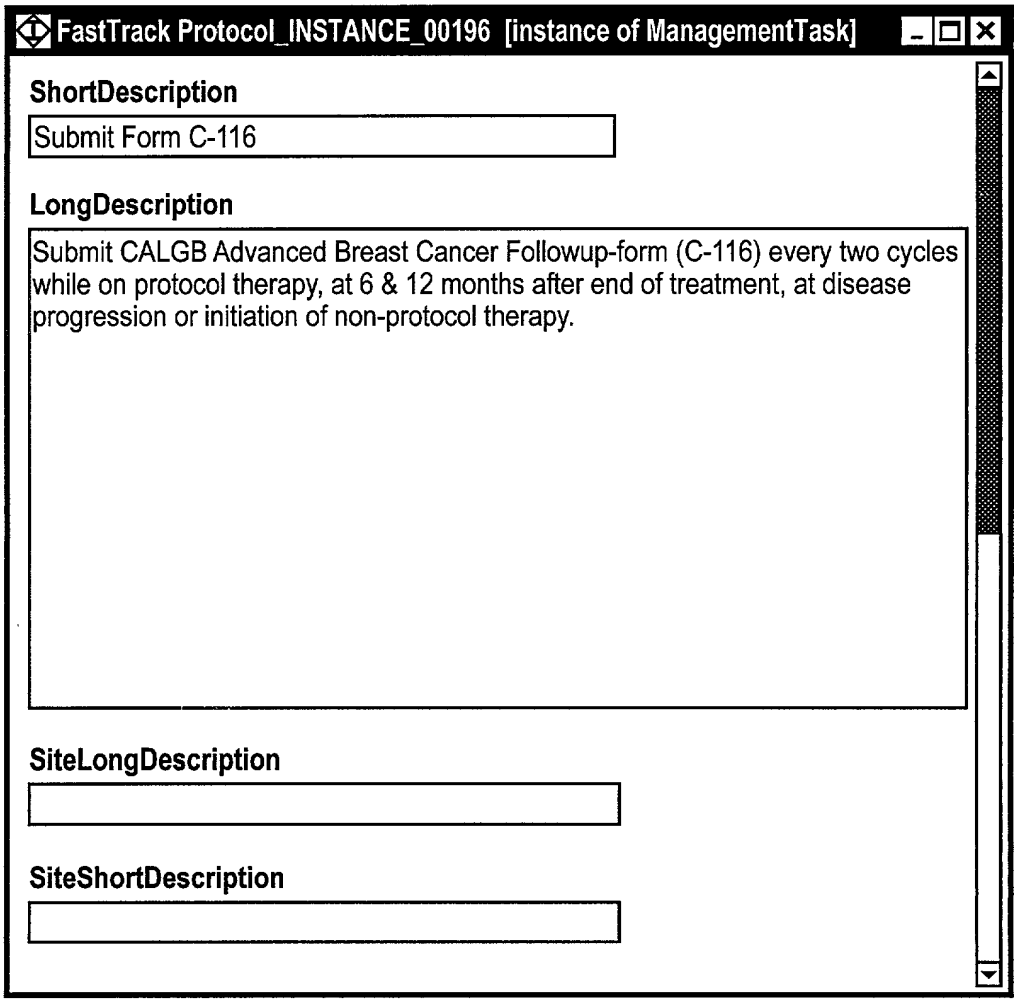
FastTrack Protocol_INSTANCE_00196 [instance of ManagementTask]
ShortDescription
Submit Form C-116
LongDescription
Submit CALGB Advanced Breast Cancer Followup-form (C-116) every two cycles while on protocol therapy, at 6 & 12 months after end of treatment, at disease progression or initiation of non-protocol therapy.
SiteLongDescription
SiteShortDescription

FIG. 21

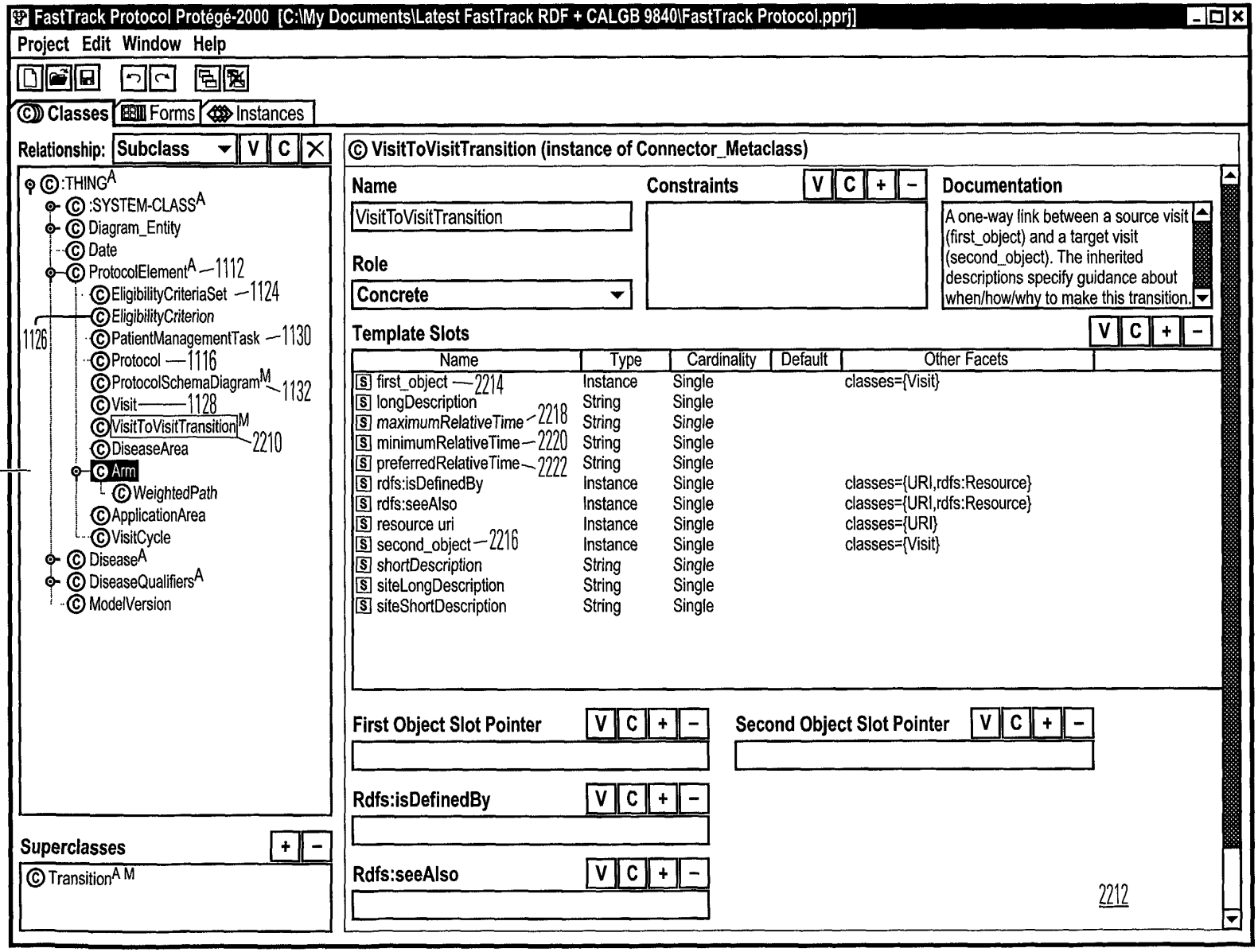
FastTrack Protocol Protégé-2000 [C:\My Documents\Latest FastTrack RDF + CALGB 9840\FastTrack Protocol.pprj]
Project Edit Window Help
Classes Forms Instances
Relationship: Subclass V C
:THING A
:SYSTEM-CLASS A
Diagram_Entity
Date
ProtocolElement A 1112
EligibilityCriteriaSet 1124
EligibilityCriterion
PatientManagementTask 1130
Protocol 1116
ProtocolSchemaDiagram M 1132
Visit 1128
VisitToVisitTransition M 2210
DiseaseArea
Arm
WeightedPath
ApplicationArea
VisitCycle
Disease A
DiseaseQualifiers A
ModelVersion
1126
1110
Superclasses
Transition A M
VisitToVisitTransition (instance of Connector_Metaclass)
Name
VisitToVisitTransition
Constraints
Documentation
A one-way link between a source visit (first_object) and a target visit (second_object). The inherited descriptions specify guidance about when/how/why to make this transition.
Role
Concrete
Template Slots
Name Type Cardinality Default Other Facets
first_object 2214 Instance Single classes={Visit}
longDescription String Single
maximumRelativeTime 2218 String Single
minimumRelativeTime 2220 String Single
preferredRelativeTime 2222 String Single
rdfs:isDefinedBy Instance Single classes={URI,rdfs:Resource}
rdfs:seeAlso Instance Single classes={URI,rdfs:Resource}
resource uri Instance Single classes={URI}
second_object 2216 Instance Single classes={Visit}
shortDescription String Single
siteLongDescription String Single
siteShortDescription String Single
First Object Slot Pointer
Second Object Slot Pointer
Rdfs:isDefinedBy
Rdfs:seeAlso
2212

FIG. 22

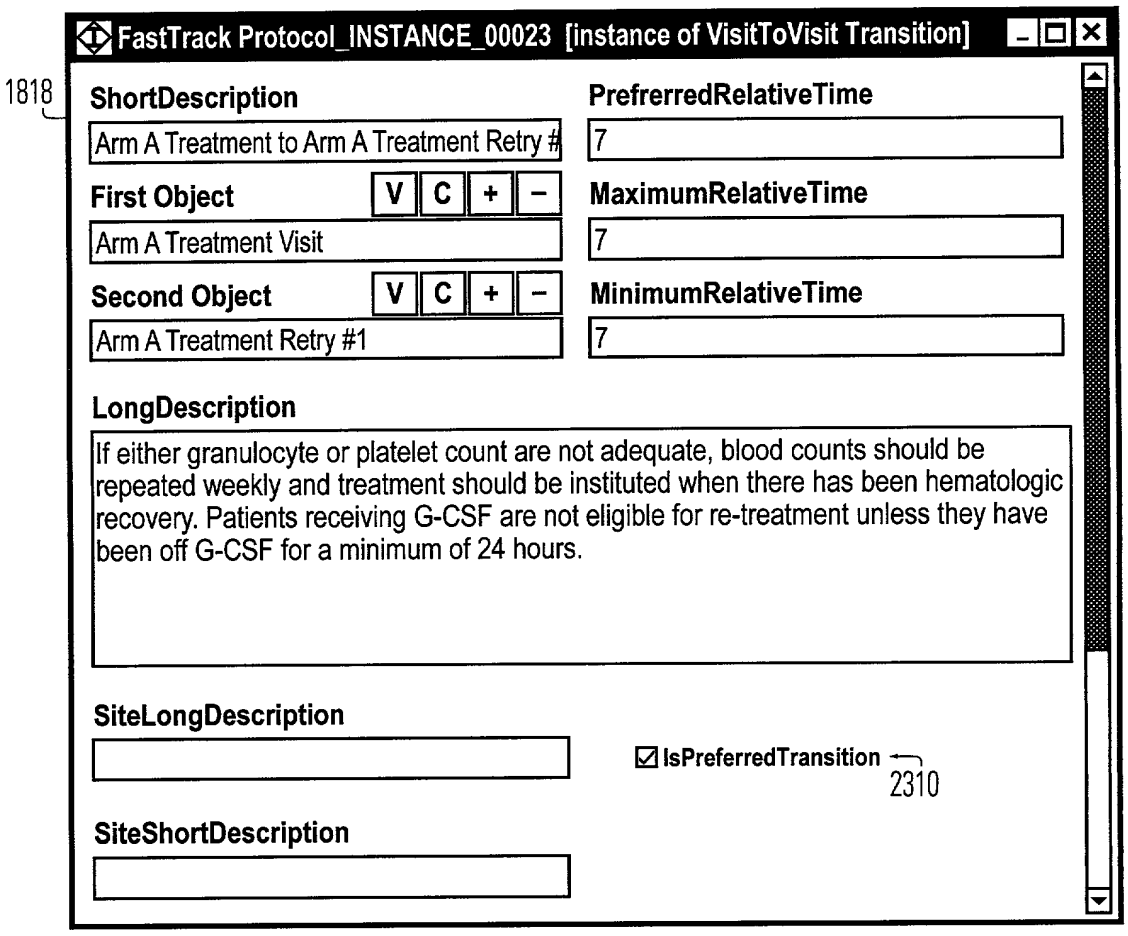
FastTrack Protocol_INSTANCE_00023 [instance of VisitToVisit Transition]
1818
ShortDescription
Arm A Treatment to Arm A Treatment Retry #
PrefrerredRelativeTime
7
First Object
V
C
+
−
Arm A Treatment Visit
MaximumRelativeTime
7
Second Object
V
C
+
−
Arm A Treatment Retry #1
MinimumRelativeTime
7
LongDescription
If either granulocyte or platelet count are not adequate, blood counts should be repeated weekly and treatment should be instituted when there has been hematologic recovery. Patients receiving G-CSF are not eligible for re-treatment unless they have been off G-CSF for a minimum of 24 hours.
SiteLongDescription
IsPreferredTransition
2310
SiteShortDescription

FIG. 23

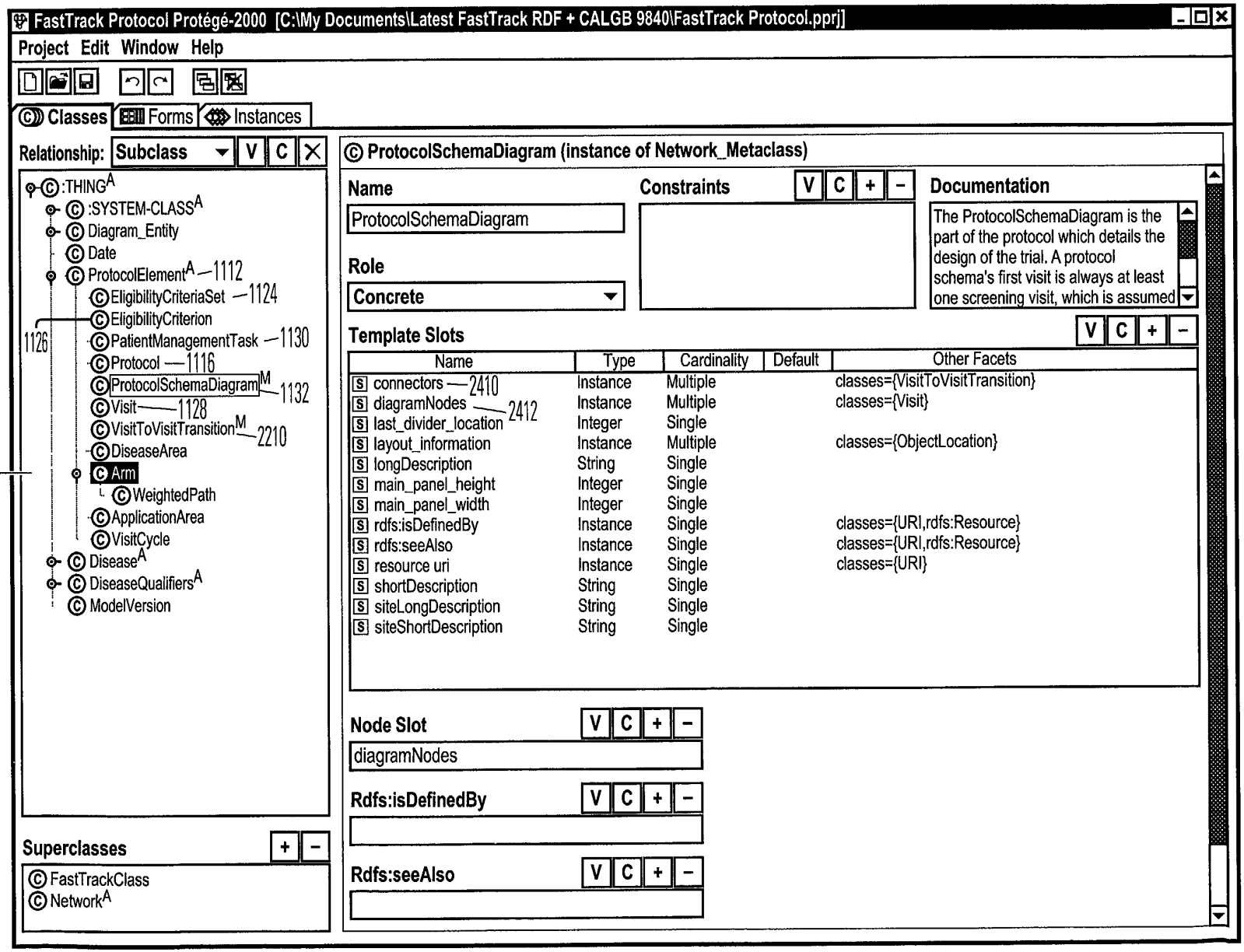
FastTrack Protocol Protégé-2000 [C:\My Documents\Latest FastTrack RDF + CALGB 9840\FastTrack Protocol.pprj]
Project Edit Window Help
Classes Forms Instances
Relationship: Subclass V C
:THING A
:SYSTEM-CLASS A
Diagram_Entity
Date
ProtocolElement A 1112
EligibilityCriteriaSet 1124
EligibilityCriterion
1126
PatientManagementTask 1130
Protocol 1116
ProtocolSchemaDiagram M 1132
Visit 1128
VisitToVisitTransition M 2210
DiseaseArea
Arm
1110
WeightedPath
ApplicationArea
VisitCycle
Disease A
DiseaseQualifiers A
ModelVersion
Superclasses + -
FastTrackClass
Network A
ProtocolSchemaDiagram (instance of Network_Metaclass)
Name
ProtocolSchemaDiagram
Role
Concrete
Constraints V C + -
Documentation
The ProtocolSchemaDiagram is the part of the protocol which details the design of the trial. A protocol schema's first visit is always at least one screening visit, which is assumed
Template Slots V C + -
Name | Type | Cardinality | Default | Other Facets
connectors 2410 | Instance | Multiple | | classes={VisitToVisitTransition}
diagramNodes 2412 | Instance | Multiple | | classes={Visit}
last_divider_location | Integer | Single | |
layout_information | Instance | Multiple | | classes={ObjectLocation}
longDescription | String | Single | |
main_panel_height | Integer | Single | |
main_panel_width | Integer | Single | |
rdfs:isDefinedBy | Instance | Single | | classes={URI,rdfs:Resource}
rdfs:seeAlso | Instance | Single | | classes={URI,rdfs:Resource}
resource uri | Instance | Single | | classes={URI}
shortDescription | String | Single | |
siteLongDescription | String | Single | |
siteShortDescription | String | Single | |
Node Slot V C + -
diagramNodes
Rdfs:isDefinedBy V C + -
Rdfs:seeAlso V C + -

FIG. 24

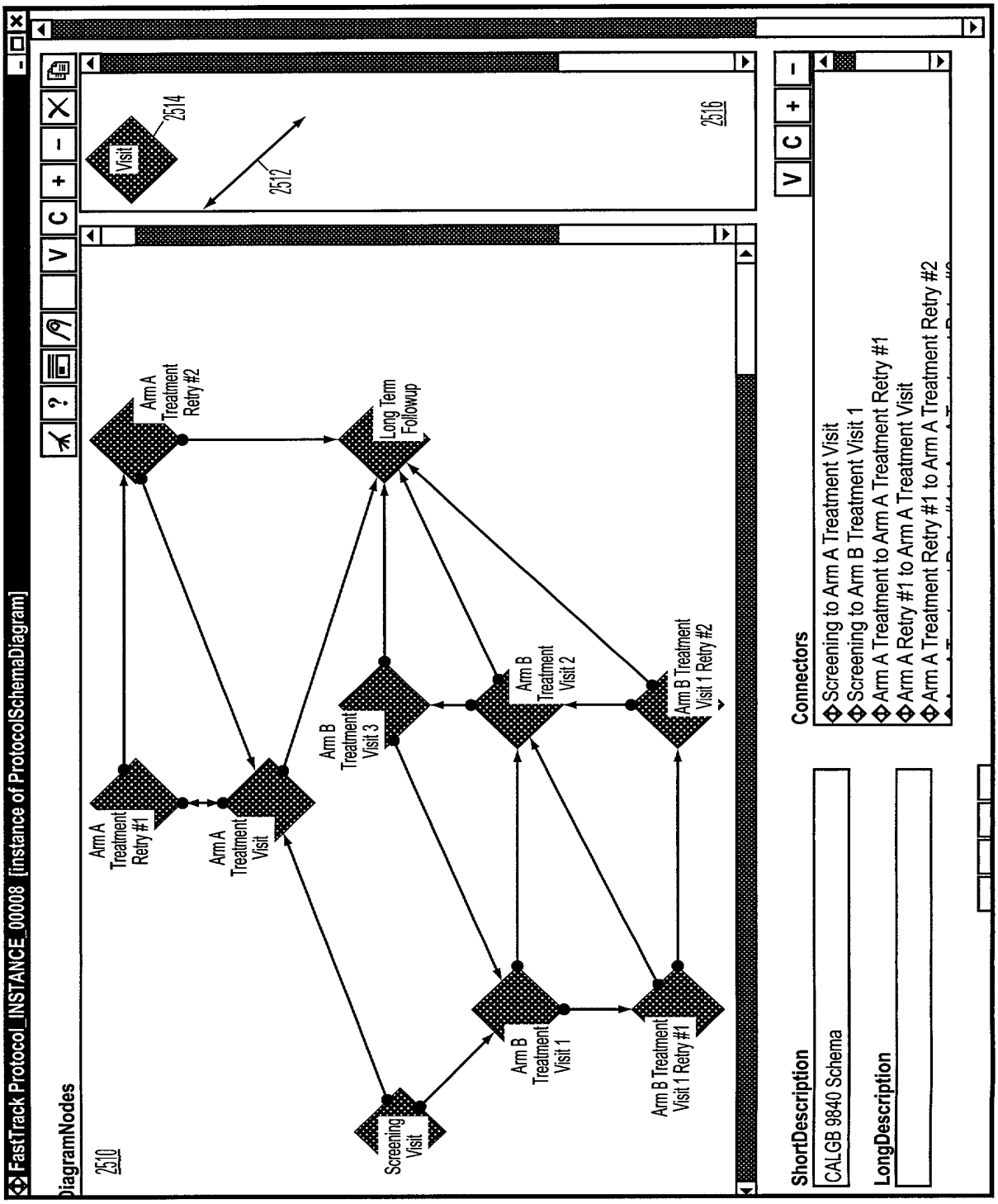
FastTrack Protocol_INSTANCE_00008 [instance of ProtocolSchemaDiagram]
DiagramNodes
2510
Arm A Treatment Retry #1
Arm A Treatment Visit
Arm A Treatment Retry #2
Long Term Followup
Arm B Treatment Visit 3
Arm B Treatment Visit 2
Arm B Treatment Visit 1 Retry #2
Screening Visit
Arm B Treatment Visit 1
Arm B Treatment Visit 1 Retry #1
2512
2514
Visit
2516
Connectors
Screening to Arm A Treatment Visit
Screening to Arm B Treatment Visit 1
Arm A Treatment to Arm A Treatment Retry #1
Arm A Retry #1 to Arm A Treatment Visit
Arm A Treatment Retry #1 to Arm A Treatment Retry #2
ShortDescription
CALGB 9840 Schema
LongDescription

FIG. 25

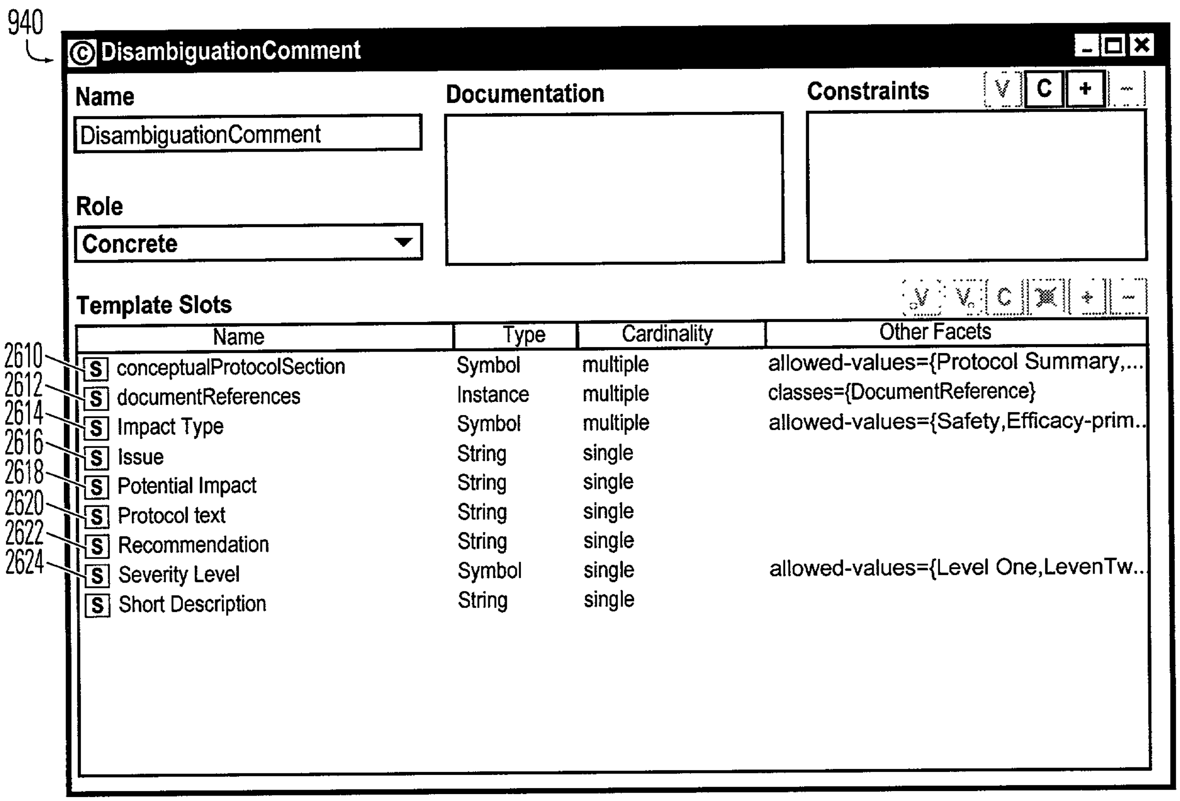

FIG. 26

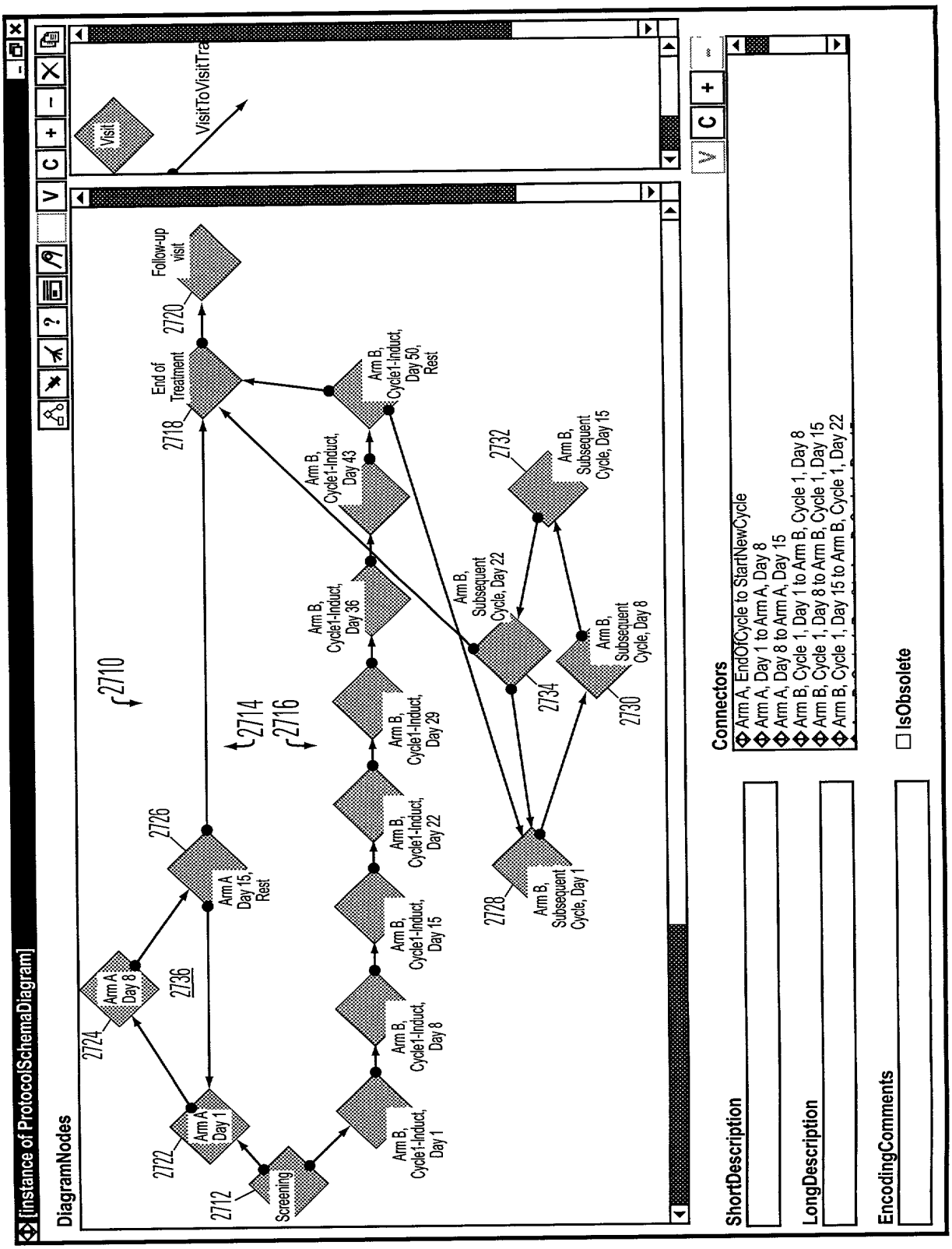

FIG. 27

Inventors: Michael G. Kahn et al.
Title: Protocol Disambiguation Using a Model-Based Methodology (as amended)
Application No. 09/974,781

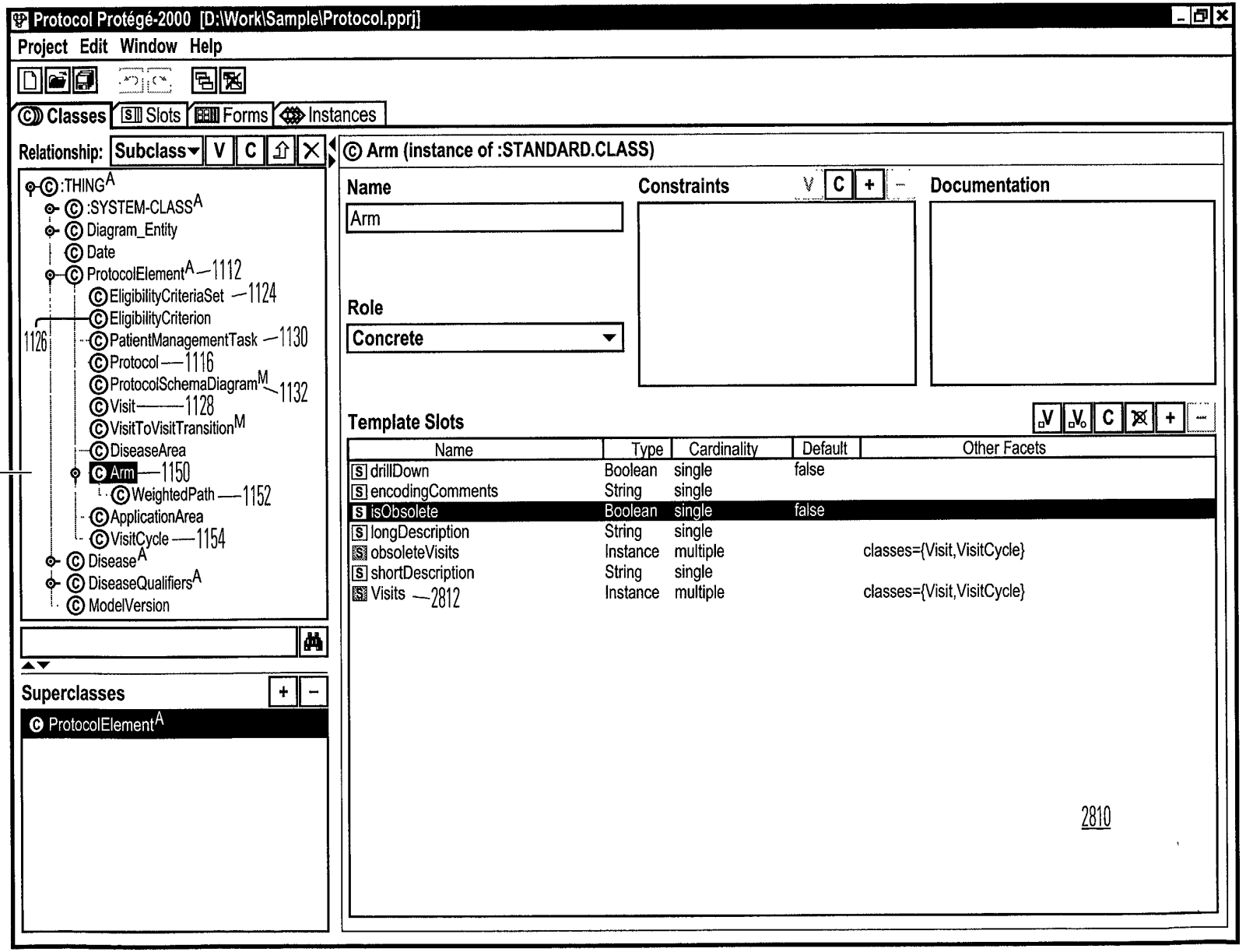

FIG. 28

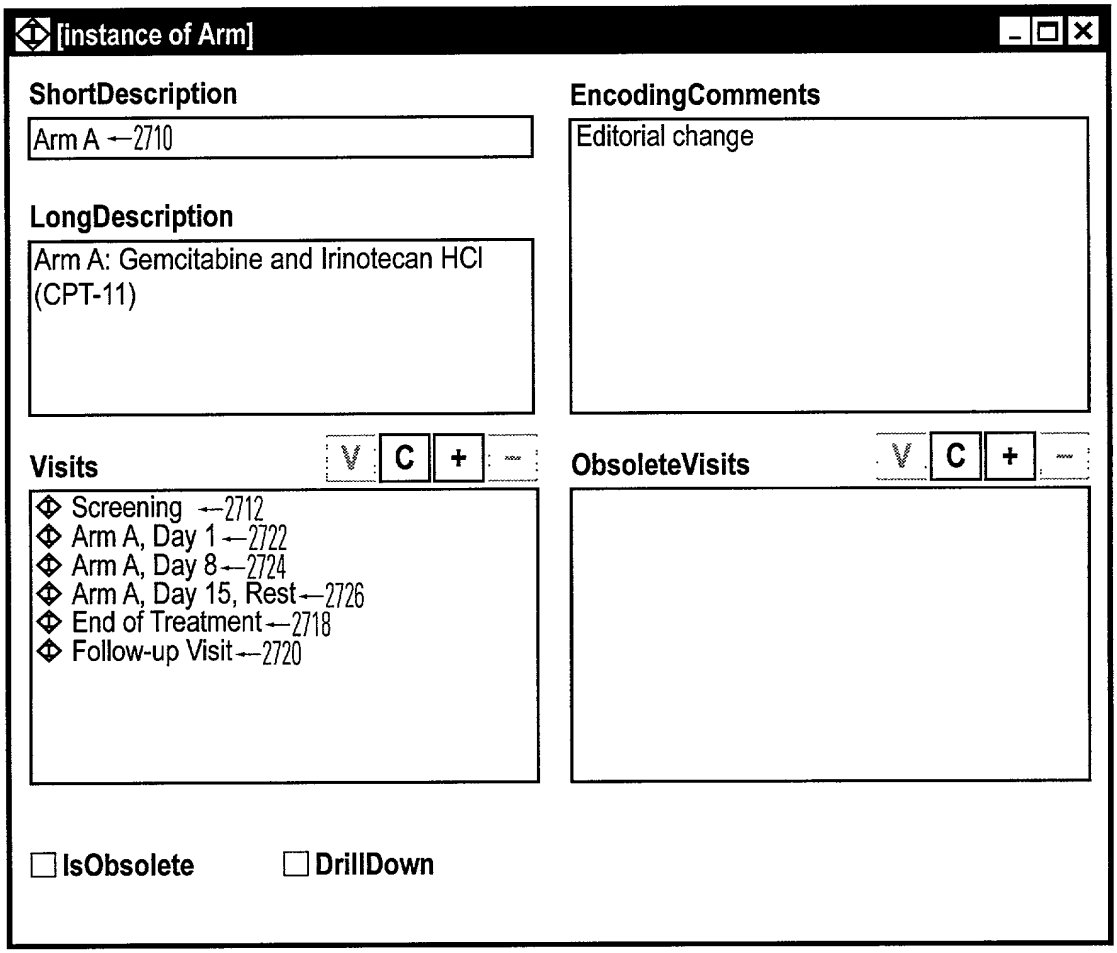
[instance of Arm]
ShortDescription
Arm A ←2710
EncodingComments
Editorial change
LongDescription
Arm A: Gemcitabine and Irinotecan HCl (CPT-11)
Visits
V
C
+
−
Screening ←2712
Arm A, Day 1 ←2722
Arm A, Day 8 ←2724
Arm A, Day 15, Rest ←2726
End of Treatment ←2718
Follow-up Visit ←2720
ObsoleteVisits
V
C
+
−
IsObsolete
DrillDown

FIG. 29

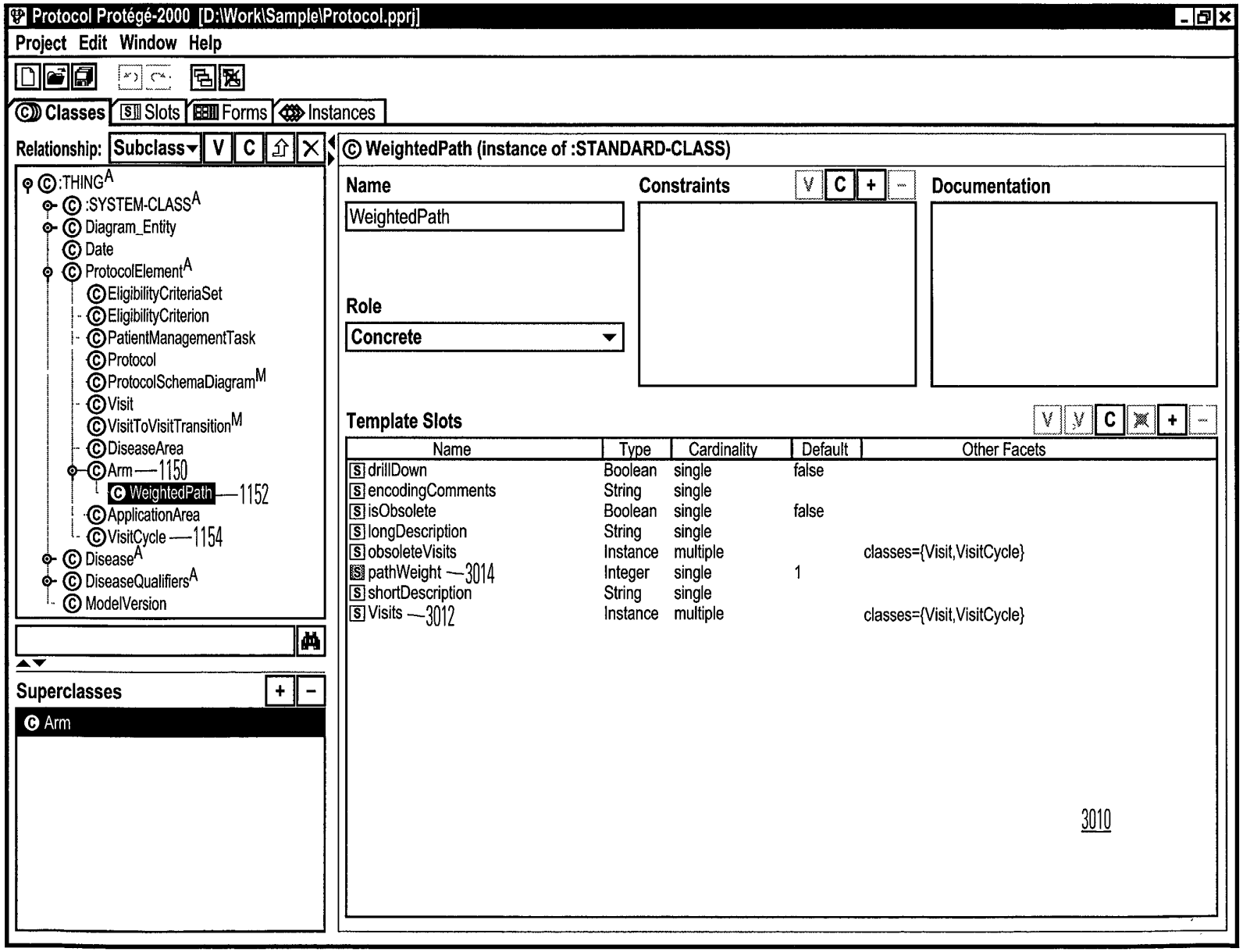

FIG. 30

Inventors: Michael G. Kahn et al.
Title: Protocol Disambiguation Using a Model-Based Methodology (as amended)
Application No. 09/974,781

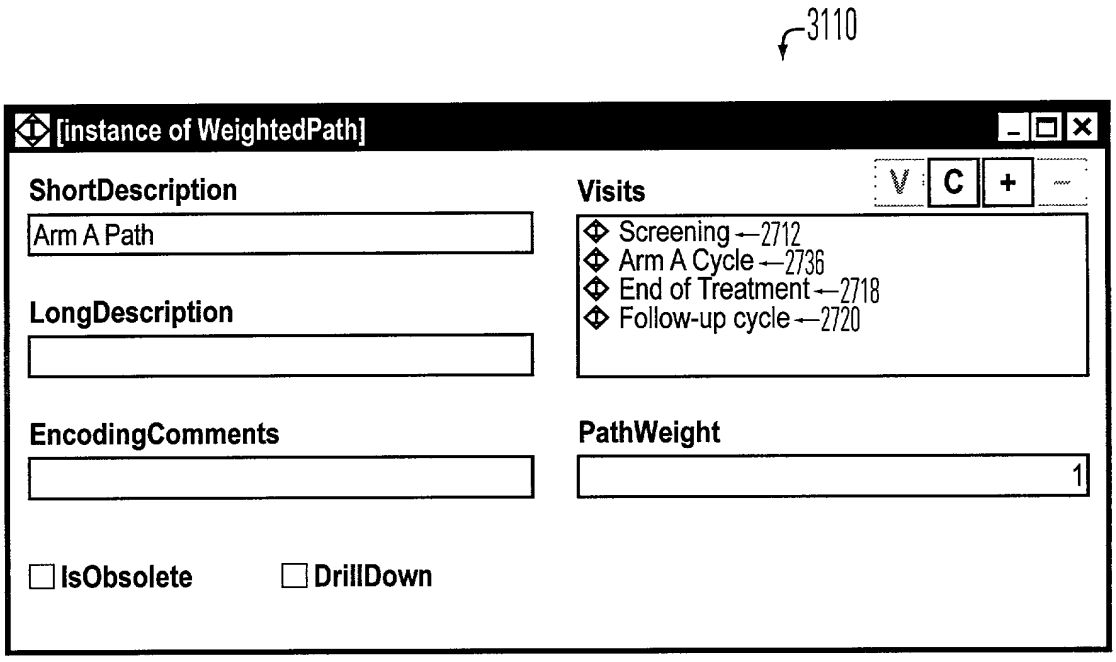
3110
[instance of WeightedPath]
ShortDescription
Arm A Path
LongDescription
EncodingComments
Visits
V
C
+
Screening
2712
Arm A Cycle
2736
End of Treatment
2718
Follow-up cycle
2720
PathWeight
1
IsObsolete
DrillDown

FIG. 31

Inventors: Michael G. Kahn et al.
Title: Protocol Disambiguation Using a Model-Based Methodology (as amended)
Application No. 09/974,781

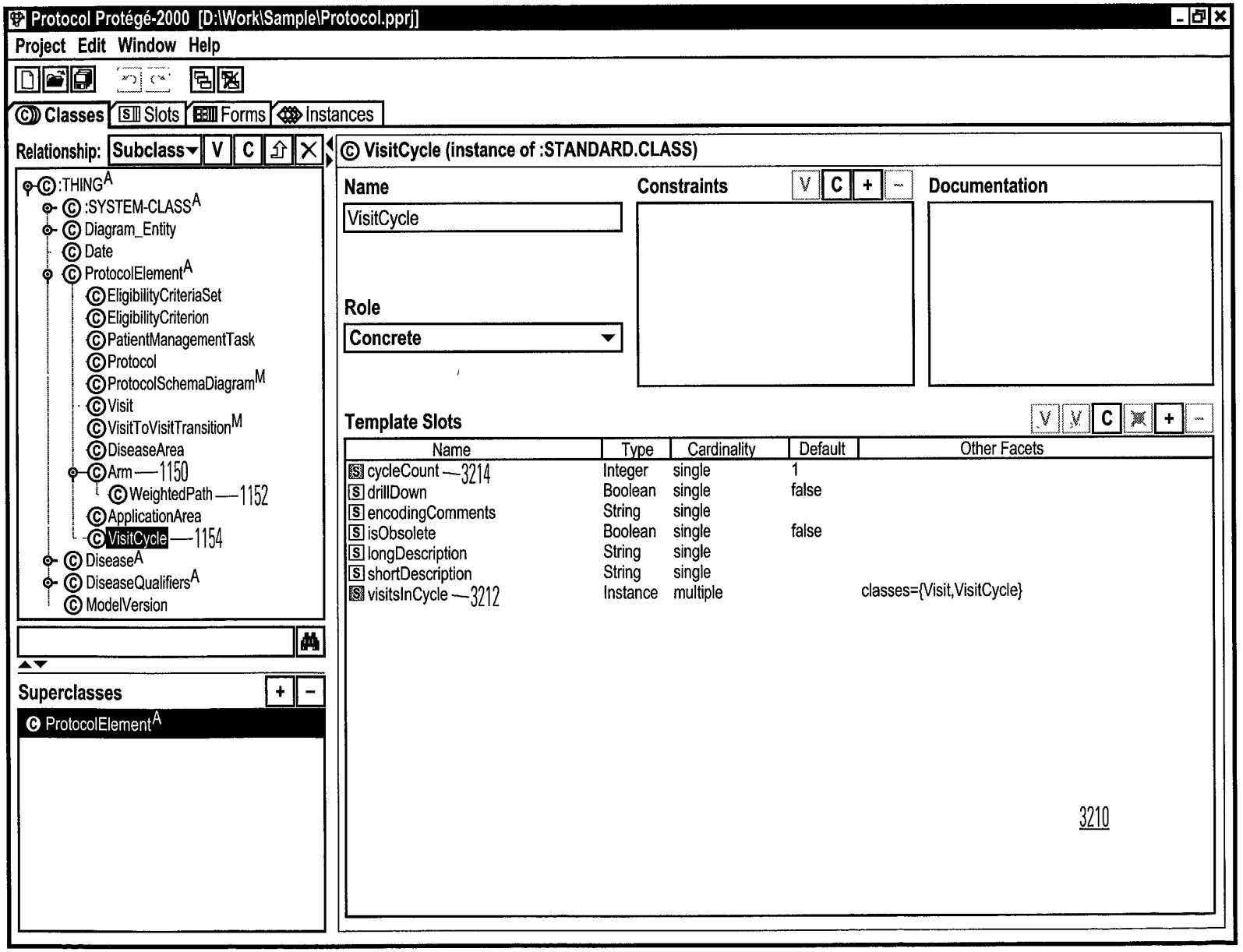

FIG. 32

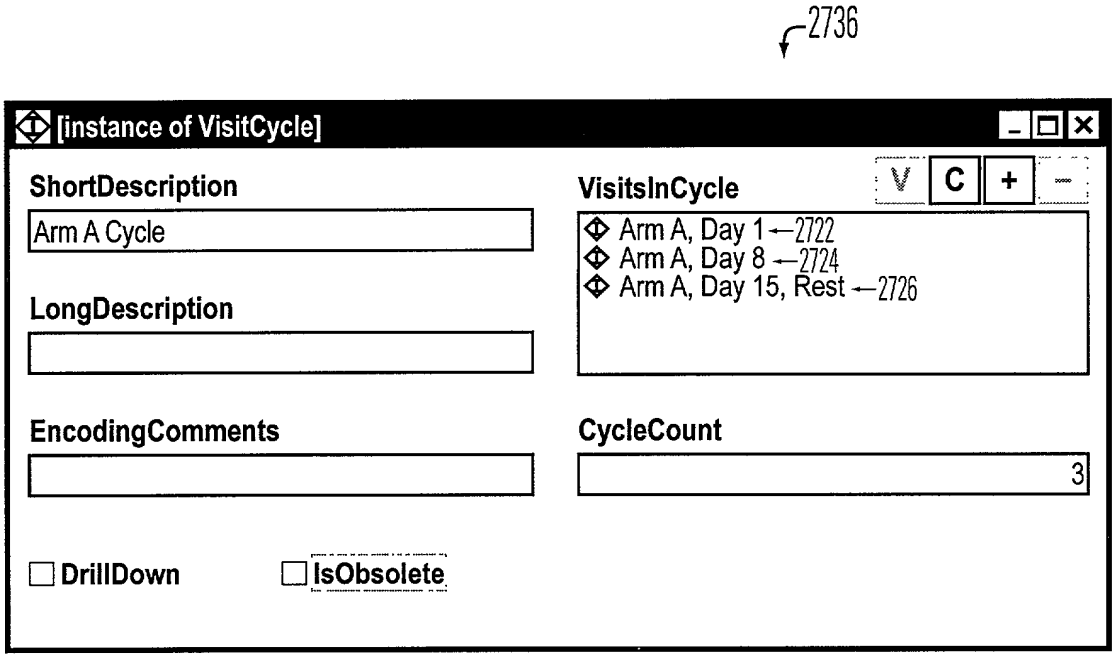
2736
[instance of VisitCycle]
ShortDescription
Arm A Cycle
LongDescription
EncodingComments
VisitsInCycle
V
C
+
–
Arm A, Day 1 2722
Arm A, Day 8 2724
Arm A, Day 15, Rest 2726
CycleCount
3
DrillDown
IsObsolete

FIG. 33

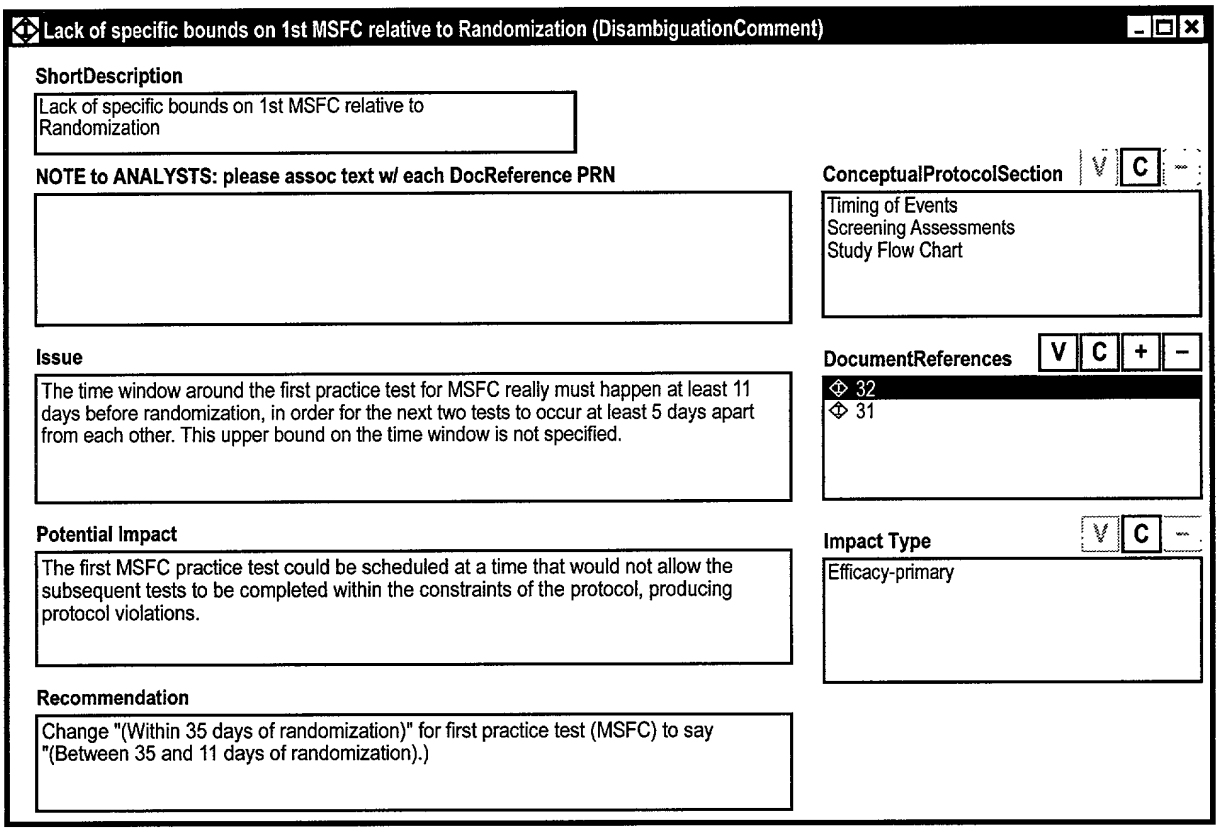
Lack of specific bounds on 1st MSFC relative to Randomization (DisambiguationComment)
ShortDescription
Lack of specific bounds on 1st MSFC relative to Randomization
NOTE to ANALYSTS: please assoc text w/ each DocReference PRN
ConceptualProtocolSection
V
C
Timing of Events
Screening Assessments
Study Flow Chart
Issue
The time window around the first practice test for MSFC really must happen at least 11 days before randomization, in order for the next two tests to occur at least 5 days apart from each other. This upper bound on the time window is not specified.
DocumentReferences
V
C
+
–
32
31
Potential Impact
The first MSFC practice test could be scheduled at a time that would not allow the subsequent tests to be completed within the constraints of the protocol, producing protocol violations.
Impact Type
V
C
Efficacy-primary
Recommendation
Change "(Within 35 days of randomization)" for first practice test (MSFC) to say "(Between 35 and 11 days of randomization).)

FIG. 34

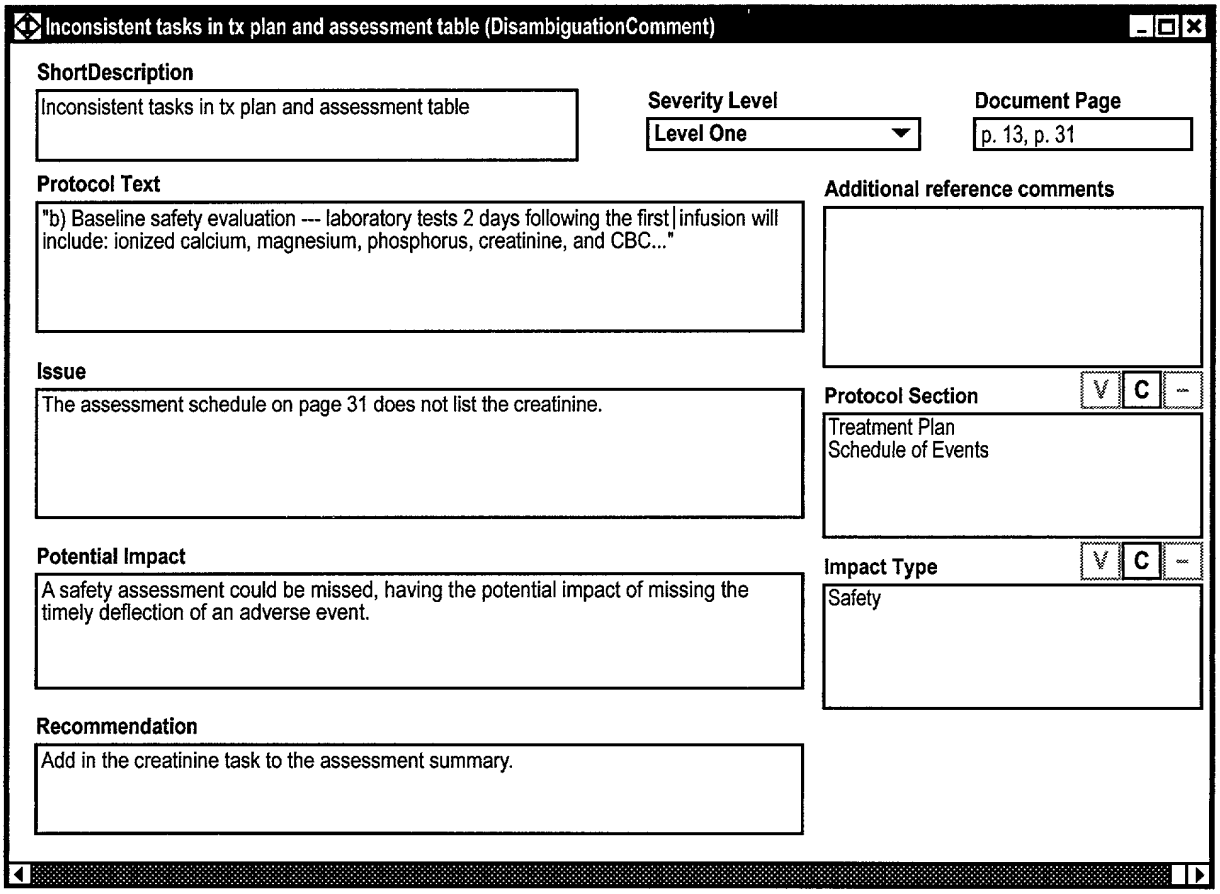
Inconsistent tasks in tx plan and assessment table (DisambiguationComment)
ShortDescription
Inconsistent tasks in tx plan and assessment table
Severity Level
Level One
Document Page
p. 13, p. 31
Protocol Text
"b) Baseline safety evaluation --- laboratory tests 2 days following the first infusion will include: ionized calcium, magnesium, phosphorus, creatinine, and CBC..."
Additional reference comments
Issue
The assessment schedule on page 31 does not list the creatinine.
Protocol Section
V
C
Treatment Plan
Schedule of Events
Potential Impact
A safety assessment could be missed, having the potential impact of missing the timely deflection of an adverse event.
Impact Type
V
C
Safety
Recommendation
Add in the creatinine task to the assessment summary.

FIG. 35

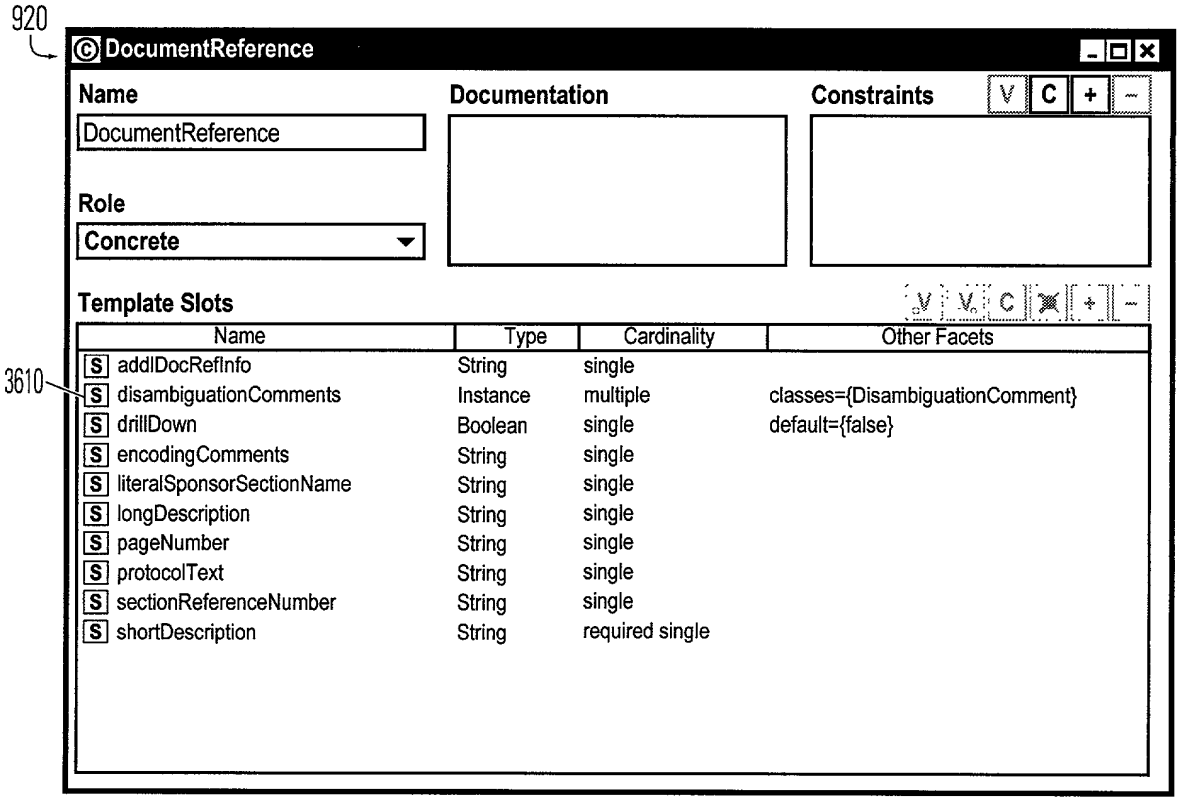
920
DocumentReference
Name
DocumentReference
Documentation
Constraints
V
C
+
-
Role
Concrete
Template Slots
3610
Name
Type
Cardinality
Other Facets
S addlDocRefInfo String single
S disambiguationComments Instance multiple classes={DisambiguationComment}
S drillDown Boolean single default={false}
S encodingComments String single
S literalSponsorSectionName String single
S longDescription String single
S pageNumber String single
S protocolText String single
S sectionReferenceNumber String single
S shortDescription String required single

FIG. 36

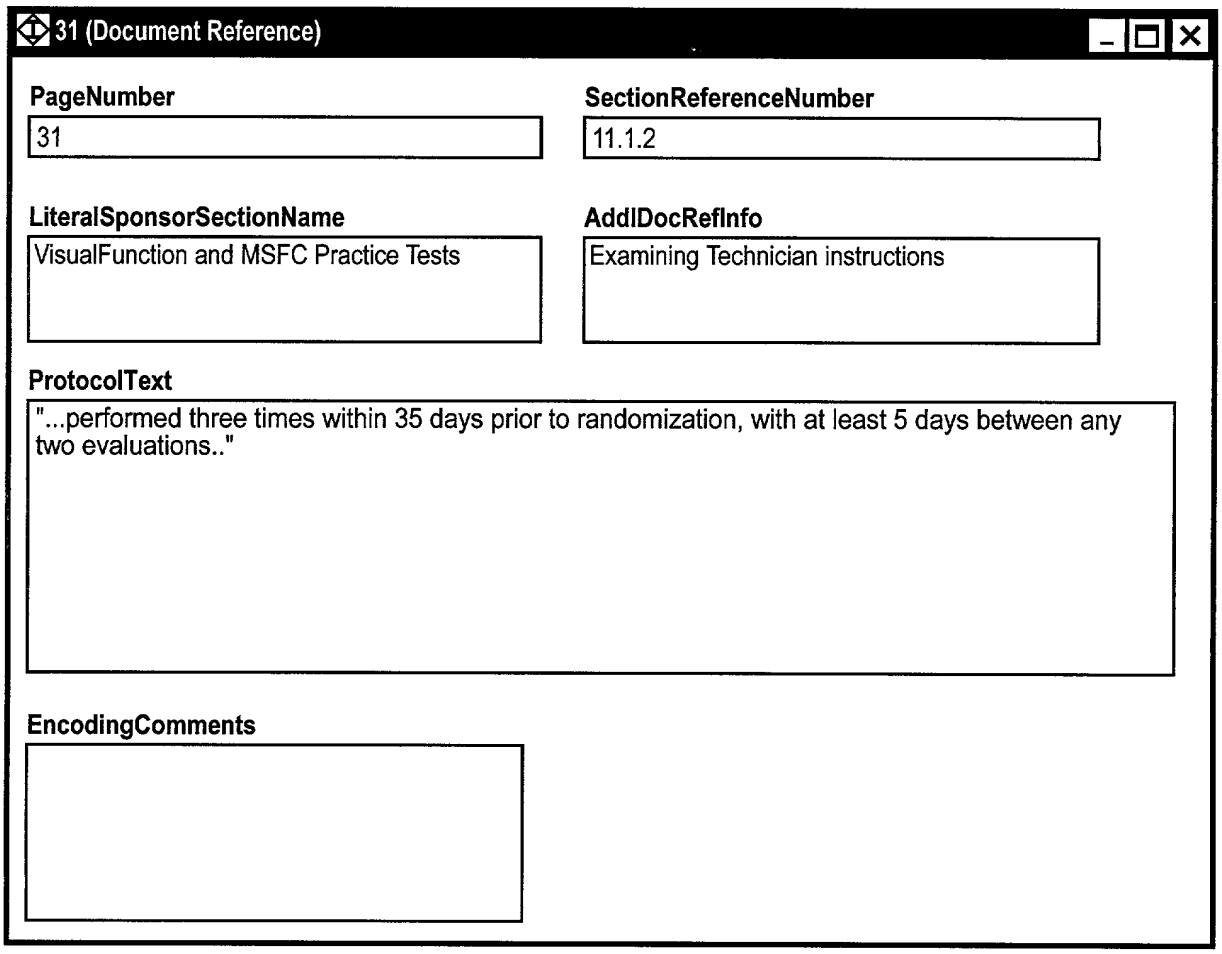
31 (Document Reference)
PageNumber
31
SectionReferenceNumber
11.1.2
LiteralSponsorSectionName
VisualFunction and MSFC Practice Tests
AddlDocRefInfo
Examining Technician instructions
ProtocolText
"...performed three times within 35 days prior to randomization, with at least 5 days between any two evaluations.."
EncodingComments

FIG. 37

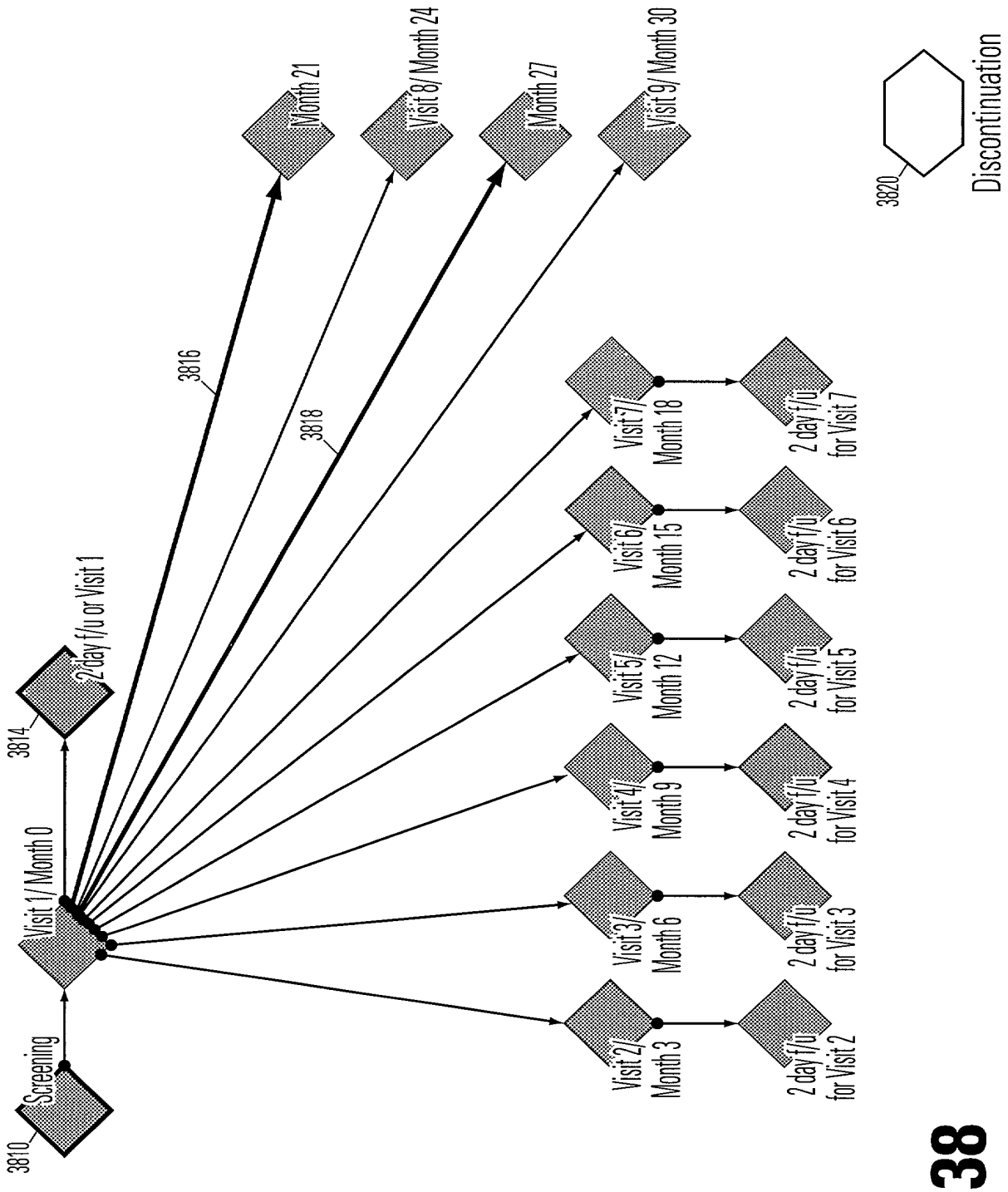
Screening
3810
Visit 1/ Month 0
3814
2 day f/u or Visit 1
3816
3818
Month 21
Visit 8/ Month 24
Month 27
Visit 9/ Month 30
Visit 2/ Month 3
Visit 3/ Month 6
Visit 4/ Month 9
Visit 5/ Month 12
Visit 6/ Month 15
Visit 7/ Month 18
2 day f/u for Visit 2
2 day f/u for Visit 3
2 day f/u for Visit 4
2 day f/u for Visit 5
2 day f/u for Visit 6
2 day f/u for Visit 7
3820
Discontinuation

FIG. 38

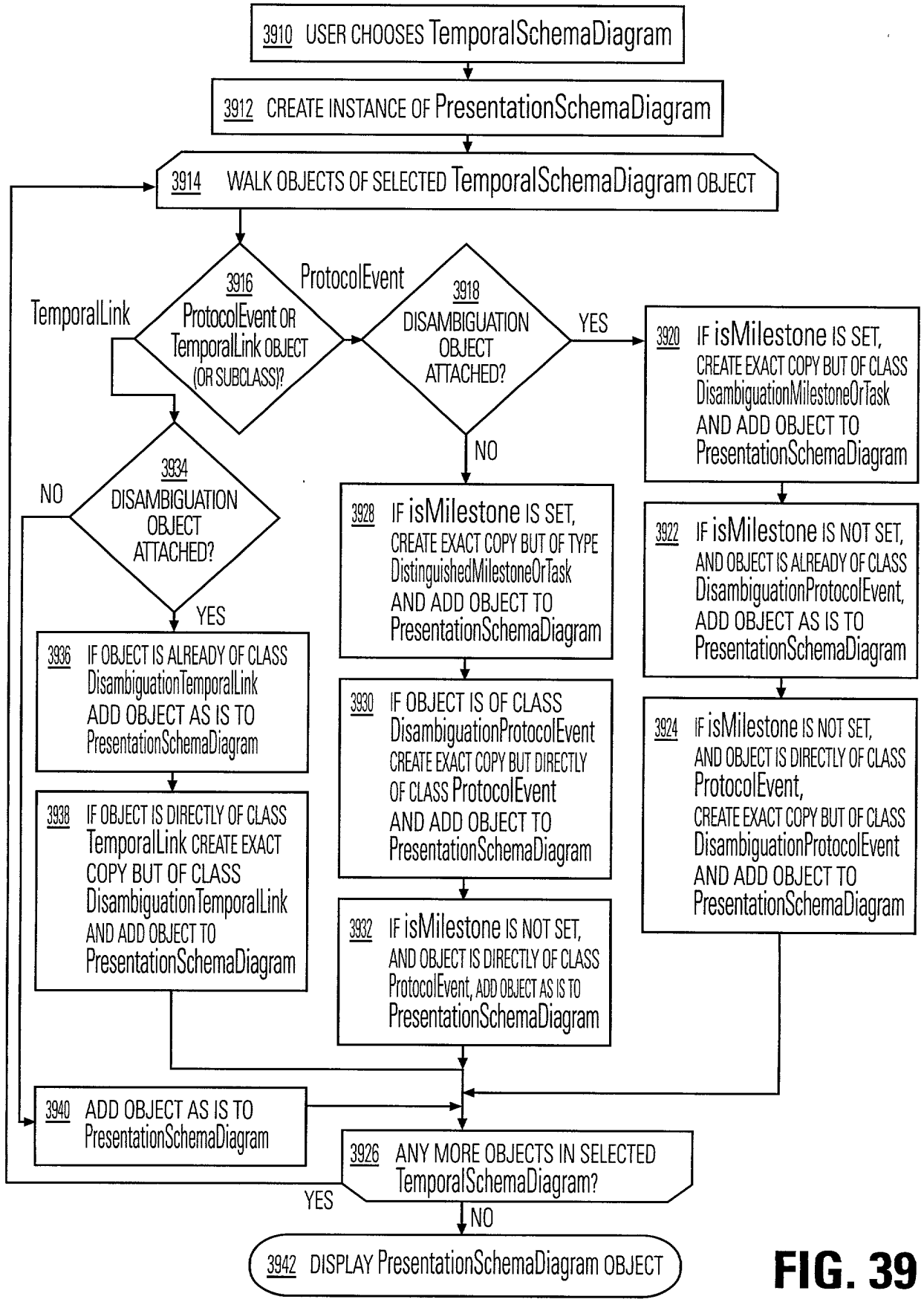

FIG. 39

DISAMBIGUATION FINDINGS

Item	Impact Type	Protocol Section	Description	Document Reference
1	Safety Efficacy-primary Efficacy-secondary	Protocol Summary Study Flow Chart	**Issue:** The description in the Protocol Synopsis of when assessments should be performed after 16 weeks is not consistent with Appendix I Schedule of Assessments. **Potential Impact:** Confusion as to when to perform these evaluations (clinical parameters and safety assessments) could result in inconsistent and inaccurate collection of data for the study. **Recommendation:** Revise sentence in the Protocol Synopsis to read, "After 16 weeks these evaluations will be performed every two to "four" months…" in order to be consistent with the timepoints indicated in Appendix I Schedule of Assessments.	*Pg. 12; Section Protocol Synopsis; Procedure; Paragraph 6:* "Clinical parameters (ACR core set) and safety assessments (adverse events and laboratory parameters) will be performed at baseline and then at monthly intervals up to 16 weeks. After 16 weeks these evaluations will be performed every two to three months, up to 104 weeks."

FIG. 40

Item	Impact Type	Protocol Section	Description	Document Reference
4	Safety Accrual	Screening Assessments Study Flow Chart	**Issue:** The protocol text specifies that if an analysis with evidence of seropositivity was performed within 6 months before screening, then rheumatoid factor testing will not have to be performed at screening. However, this is not noted in Appendix I Schedule of Assessments. **Potential Impact:** Unnecessary analysis performed at screening. **Recommendation:** Add a footnote to the Rheumatoid Factor assessment in Appendix I to clarify that documented evidence of seropositivity is acceptable as screening data if obtained within 6 months before screening.	*Pg. 28; Section 8.6.2; Rheumatoid Factor:* "Unless there is documented evidence of rheumatoid factor titre within 6 months before screening a blood sample for this analysis will be taken." *Pg. 41; Section Appendix I; Schedule of Assessments*

FIG. 41